PREDICTION OF ADULT HEIGHT IN CHILDREN WITH GROWTH DISORDERS

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Thesis submitted to the Yale University School of Medicine in Partial Fulfillment of the Requirements for the Degree Doctor of Medicine

by

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ABSTRACT

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The adult heights of 119 former patients from the Yale Pediatric Endocrinology Clinic were obtained and compared to their predicted heights. All of these patients were seen for evaluation of their growth. Adult height predictions were obtained with the Bayley-Pinneau and Roche-Wainer-Thissen methods as well as with the "Genel/Lenko Method" in which bone age and current height are the predictors. The Genel/Lenko method was found to have a larger error than the other two methods and to overpredict in most cases. The RWT method was the most precise, although often not the most accurate method. The largest diagnostic group in the series consisted of boys with constitutional delay; the RWT method was the most reliable for this group.

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Myron Genel originated the idea for this project and provided encouragement and guidance throughout. He also demonstrated careful attention to the concerns of patients with growth disorders which was (as many former patients noted) of lasting benefit to them.

Robert McDonald provided invaluable computer technology and many hours of patient assistance in its application. He deserves special thanks for help with graphs, tables, and page numbers, and for providing reassurance at several key moments during this project.

The 119 participants in this study provided me with measurements, often at the expense of considerable time and effort. Their willingness (and that of many of their family members) to participate in the study made the data collection phase of this project enjoyable, and greatly increased my appreciation of the clinical importance of height prediction.

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I. INTRODUCTION

It has long been of interest to parents to try to estimate their children's adult height. Whether or not a child will reach the same height as his father or mother is a matter of at least passing interest in most families. For those who develop a serious interest in a career or sport which involves a height restriction (e.g., police, pilots, gymnastics, ballet or basketball), there may be concern about planning for such a goal.

Similarity to peers is an important concern for children, especially during adolescence, when they are most likely to differ in stature and rate of development. Short stature may lead to feelings of anxiety and inferiority, resulting in withdrawal or other undesirable compensatory behavior. Even normal shortness can be a cause for concern, because it is often perceived (by both children and parents) to have an adverse effect on a person's future.

The personality development of children with hypopituitary growth hormone deficiency has been studied (Rotnem et al., 1977). These children were found to suffer from disturbances of identity formation, body image, and difficulties in the expression of feelings of aggression and incompetence. Such disturbances are believed to arise from social and emotional immaturity resulting from the nature of social interactions elicited by short stature. These

children were often treated in a manner suitable for much younger children, even by adults such as parents and health care personnel who were aware of their actual age and interested in treating these children appropriately. Parents were found to underestimate the developmental difficulties of these children and to treat them with overprotectiveness and a controlling parental style (Rotnem et al., 1977).

For many years, the supply of human growth hormone was derived entirely from a limited supply of cadaver pituitaries, and its use was restricted to children with severe growth hormone deficiency. The supply was withdrawn in early 1985 after the deaths of four people who had received pituitary-derived GH were reported. The cause of death was Creutzfeld-Jacob disease, which is believed to be transmitted by infectious material from human brains. Six months later, the first GH preparation produced with recombinant DNA technology (Protropin) was approved by the FDA for treatment of GH deficiency. This biosynthetic GH differs from native GH by one amino acid (containing an additional methionine) and has been shown to be effective in treatment of children with GH deficiency (Kaplan et al., 1986). A second biosynthetic GH (Humatrope) is now available; its amino acid sequence is identical to that of endogenous GH. Although GH is no longer scarce, it is still very expensive; one year of treatment may cost over $13,000 (Wilson and Rosenfeld, 1987).

The efficacy of treating children with growth hormone deficiency has been well established; however, its use in genetically short but otherwise normal children has not been clearly demonstrated. While there is evidence for some short-term increase in growth rate with GH treatment (Gertner et al., 1984), no long term benefit has been shown for such children. The possible side effects of GH treatment with pharmacologic doses in children who are not deficient are not known. Based on information from patients with acromegaly, side effects may include hypothyroidism, formation of potentially growth-limiting antibodies to GH, glucose intolerance, hyperlipidemia, and acceleration of atherosclerosis (Underwood, 1984). Therefore, the need for GH treatment should be assessed as carefully as possible.

In addition to the medical concerns, there are considerable psychosocial issues as well. Society places an enormous value on height; it is a commonly held view that taller people are more successful, earn more money, and are more attractive than shorter people. The bias toward tall people may in fact be as widespread as racism and sexism, although its effects are perhaps more subtle. It is inevitable that enormous pressure will be exerted on pediatricians to treat healthy children who are genetically short, or whose growth tempo lags behind the mean (in spite of an average ultimate height potential). In most cases, these children will be technically normal (taller than the

third percentile for age); however, their parents may be eager to protect them from the effects of "heightism". Parents may also seek treatment for children who do not meet expectations for athletic achievement, or even academic or social accomplishment, and in these instances, successful treatment seems unlikely, even if an increase in stature is achieved.

In evaluating the risks and benefits of GH treatment, the possibly adverse psychosocial effect of undergoing multiple physician visits and receiving three injections every week should also be considered. In one study of 11 GH deficient children who received one year of GH therapy, the majority at least doubled their pretreatment growth rate. However, the increased growth was less than anticipated by the children and their parents (Rotnem et al., 1979). This "relative treatment failure" was manifested by an emergence of depressive themes in psychological testing which had not been apparent before treatment. Decreased self-esteem, withdrawal, and anger were also evident after treatment. Expectations of growth were believed to have been increased with extensive endocrine evaluations and hospital admissions. Despite the children's disappointment, in most cases, physicians considered the treatment successful (Rotnem et al., 1979). In view of these findings, it seems that reliable prediction of adult height and expected treatment outcome are crucial to providing appropriate counseling to

children before undertaking a course of GH therapy.

In addition to being used for evaluating the need for treatment and counseling patients, predictions of adult height have also been used to assess short-term effects of treatment of growth disorders (Colle et al., 1977, Martinez et al., 1987; Schoenle et al., 1987). While the only completely reliable means for evaluating the efficacy of treatment is to compare the adult heights of a treated group to those of a non-treated group, this requires years of followup and is often not practical. Since different prediction methods may produce different biases for certain groups, the choice of a prediction method could result in an erroneous demonstration of the efficacy of a treatment method. For example, if a prediction method tends to underpredict adult height for children of a certain age (e.g., when treatment begins), but not for later ages (e.g., when treatment ceases), then by comparing the adult height predictions before treatment (underpredictions) to after treatment (more accurate), a treatment method could be erroneously considered to be effective.

An illustration of this is provided by a study in which height predictions were done before and after testosterone treatment of boys with constitutional delay, and adult heights were also obtained (Martin et al., 1986). Although pre- and post-treatment predictions were equivalent, the group which received the highest testosterone dose failed to

achieve their predicted heights by a statistically significant margin. This was due to a decreased growth rate after treatment ended. If the treatment had been evaluated solely on the basis of height predictions, high dose therapy would have been considered effective for inducing a growth spurt, when it actually was associated with a decrease in adult height.

The height prediction methods currently in use were developed with data from normal children (with the exception of the method of Lyon et al. (1985) for Turner's Syndrome). The accuracy of the prediction methods for children with growth disorders must be assessed in order to evaluate the effects of treatment.

Growth curves have long been used as indicators of disease and as a means of following patients with chronic diseases (e.g. congenital heart disease, chronic renal insufficiency). Patients who receive growth-inhibiting medications (e.g. steroids) also need to have their growth followed carefully. Management of these patients would be easier with reliable, accurate means of adult height prediction.

II. BACKGROUND

A. Skeletal Age Estimation as a Measurement of Maturity

All of the commonly used methods of adult height prediction include an estimation of skeletal age (or bone age). Because there have been many methods proposed for this purpose, a discussion of height prediction necessarily begins with a review of these methods. The concept of bone age originated as an attempt to quantify maturation. Bone age has been defined as the age at which the radiographically observed bone maturation is average (Schaff-Blass et al., 1984). Maturity differs from other anthropometric measurements, such as stature, in that every individual progresses from a state of complete immaturity to one of maturity. Stature and other size measurements do not define maturity; a child who is "tall for his age" may be more mature than his peers, or he may simply be a tall child of average maturity who will be a tall adult.

1. Atlas Methods of Skeletal Age Estimation

The atlas methods involve comparison of a patient's radiograph (usually of the hand-wrist) to standard radiographs until one is found that matches the maturity level of the patient. The method was developed by Todd (1937) and others who developed atlases of standards for the hand-wrist, foot-ankle, and knee (Greulich and Pyle, 1959; Pyle and Hoerr, 1969; Hoerr et al., 1962). These standards

were derived from serial radiographs of white children of high socioeconomic status in Cleveland, Ohio.

The Greulich and Pyle atlas has separate standards for boys and girls; the others have one set of standards with corresponding sex-specific bone ages. The Greulich and Pyle standards have been shown to be more advanced than samples of Finnish and Danish children as well as U.S. children between the ages of 9-13 years (Roche, 1986). This has been attributed to the high socioeconomic status of the study participants and to the unusual procedure used to establish the sex-specific standards.

The atlas method is most accurate when used to assign bone-specific ages which are combined to obtain the overall bone age. However, the more frequent technique of assessment is to obtain a subjective impression of which standard best matches the patient's radiograph. Because the bones in the standards themselves differ in maturity, this less systematic approach is likely to be less accurate than the bone-specific method.

Intraobserver differences between repeated readings are about 0.5 years for experienced observers using the atlas method. Interobserver variances are about 0.8 years (Roche, 1986). These differences are comparable to the standard deviations of about 10-12 months given with the standards in the Greulich-Pyle atlas.

2. Tanner Whitehouse Method

The bone age method used in the Tanner Whitehouse height prediction method (1983, see description on pp. 14-15) is called the "RUS bone age." It is obtained by assigning a numerical score to each of the 20 RUS bones (radius, ulna, and short finger bones); the average score provides an overall maturity estimate. Approximately nine radiographically defined stages are used as maturity indicators. This method was designed to quantify maturity more objectively than the atlas method.

3. Roche Wainer Thissen Method

Roche and colleagues developed a method for bone age estimation based on the assessment of 34 maturity indicators for the femur, tibia, and fibula. A computer program analyzes these and provides a skeletal age estimate with a standard error. Reliability is reported to be comparable to the RUS bone age and better than the hand-wrist atlas methods (Roche et al., 1975; Roche, 1986). For convenience, however, the RWT height prediction method uses the Greulich-Pyle hand-wrist bone age. No height prediction methods have been developed for use with the knee bone age.

B. Methods of Height Prediction

The ideal method for height prediction would be statistically reliable (i.e., both accurate and precise), inexpensive, easy, rapid (i.e., could be accomplished in one visit), applicable to a clinically relevant age group, and

applicable to different diagnoses (or have a known bias for different diagnoses). As discussed below, the various methods which have been proposed for clinical use vary in the degree to which they fulfill the above characteristics. Most methods provide data for accuracy and precision in the "standardizing group" (population with which the method was developed) and at least one "validating group" (not used to develop the prediction method). Accuracy is generally assessed by mean prediction error (predicted height minus adult height), and precision by the standard deviation of the mean prediction error. As expected, heights of children from the standardizing population are predicted with the greatest accuracy and precision.

The most commonly used methods of height prediction are referred to by the following abbreviations: BP for the Bayley and Pinneau method (1952), RWT for the Roche-Wainer-Thissen method (1975), and TW2 for the method of Tanner, Whitehouse, and others (1983).

1. Bayley-Pinneau Method

This method is based on the high correlation between skeletal age and percent of adult height achieved. Children are divided into three groups: accelerated, average, or retarded in skeletal maturation, based on the difference between chronological age and skeletal age. Since the variation of chronological-skeletal age is continuous, the separation into three groups can cause large fluctuations in

serial predictions for children whose group membership changes between predictions.

The BP tables are based on data from 192 normal children (103 girls and 89 boys) who were measured and x-rayed every 6 months from 8 to 18 years (or until epiphyseal fusion occurred). The prediction errors and sample sizes for each of the three groups were not reported.

The child's current height and Greulich-Pyle bone age are used to obtain the prediction. The method may be used for most girls with bone ages of 6.0-18.0 years and most boys with bone ages of 7.0-18.5 years (the ranges vary depending on which of the three groups the patient belongs to). Accuracy is increased with serial exams and x-rays; however, a single exam may be used. For normal children, the BP method is reported to be accurate to within an inch for about two-thirds of girls through age 12 and boys through age 14. After these ages, the prediction error was less than an inch for most children, decreasing to less than 0.5 inch after age 13.5 in girls and 16 in boys (Bayley and Pinneau, 1952). The method has also been reported to underpredict in girls of all ages and to overpredict in boys at 7, 15, and 16 years (Roche et. al, 1975).

The BP tables have also been published in the Greulich-Pyle atlas (1959) and have been summarized by Post and Richman (1981). A pocket height predictor has been prepared by Genentech (a major GH manufacturer) based on these tables.

2. Roche-Wainer-Thissen Method

The RWT method predicts stature at 18 years; final adult stature can be predicted with correction factors. The method was derived using data from middle-class Ohio children born in 1929-1954. About 800 children were enrolled, with about 100 of each sex in each age group. The children were weighed, measured, and x-rayed every 6 months until age 18, with biennial exams thereafter.

A multiple regression equation is used to predict adult height from recumbent length, skeletal age (median of Greulich-Pyle bone-specific skeletal ages (Greulich & Pyle, 1959)), weight, and mid-parent stature. Although some of these variables contribute little to the adult height estimate, coefficients are given for all variables at all ages. Stature can be substituted for recumbent length with the use of a correction factor. Population means can also be substituted for other parameters, with some decrease in accuracy, depending on the importance of the particular variable for the particular age group.

The method is applicable from 1-14 years in girls, and 1-16 years in boys. It is designed to be used for children who have fewer than 50% of their hand-wrist bones judged to be mature; predictions for more mature children are felt to be unimportant because of their limited remaining growth potential. As a result, the RWT method is less accurate than BP for older children. Median absolute errors, in validation

samples, were generally less than 3 cm, and less than 6 cm for 90% of patients in both sexes. The accuracy of prediction, as a percentage of adult height, was slightly less for girls than for boys; however, since girls tend to be shorter than boys, the absolute errors of prediction were comparable. (This could become more important in predicting adult stature for girls with genetic tall stature.) The method was checked and compared to the BP method by applying both methods to two verification populations. The RWT method was found to be more accurate than BP except at older ages. The authors felt this may have been due to the inclusion of children whose hand-wrist bones were more than 50% mature. The median errors with RWT showed less variation with age than with the BP method; this was attributed to the use of more parameters in the RWT method, and the treatment of skeletal and chronological age as continuous variables. Prediction errors at puberty were notably smaller for RWT than BP, especially for girls (Roche et al., 1975).

While providing accurate predictions for the tested populations over a large age range, the RWT method is considerably more complicated than the BP method. More data are required than for the BP method, and RWT is not applicable to more mature children. (It is even possible for the RWT equation to result in a prediction for an older child which is less than the child's current height.) Since children often present for growth evaluation around puberty,

this may be a drawback for clinical use. Although there may be little growth remaining for such children, accurate height prediction may still be very useful for counseling.

3. Tanner-Whitehouse Method

The TW Mark 2 Method (TW2) was published in 1983 (Tanner et al., 1983), as a revised version of TW Mark 1 (Tanner et al., 1975). The Mark 2 method is based on data from a standardizing sample which included 260 normal British children (110 boys and 150 girls) who were followed in longitudinal growth studies, as well as 63 children (34 boys and 29 girls) attending a Growth Disorder Clinic. These children were very tall, very short, or very delayed, but were free from gross pathological conditions. For most of these children, adult height was measured at home by a family member following written instructions.

TW2 predictions are obtained with regression equations which use RUS bone age, chronological age, and stature as the variables. Separate equations are used for pre- and postmenarcheal girls. When available, equations use "increase in height during previous year" and "increase in RUS bone age during previous year" for ages at which this increases accuracy (11-15 in boys and 8-14 in girls). The method is applicable for boys from 6 to 18.5 years and girls from 5 to 16.5 years.

In the standardizing groups, TW2 is only slightly more accurate than TW1, but the range of children covered is

greater. Residual standard deviations are provided for the regression equations at each age; these range from 1.4 to 4.7 cm for boys and 0.9 to 3.7 cm for girls. This allows each prediction to be made with limits (± one standard deviation) associated with a 67% probability that the adult height will fall in the specified range. The standard deviations are smaller for the TW2 method than for RWT for children over age 12; below age 10 the RWT method is better. At ages 10 and 11 the methods are comparable. The method is designed to apply to tall, short, and delayed, as well as average children; however, no data are available on the reliability of TW2 predictions for children with pathological conditions.

The TW2 method provides an accurate means of estimating adult height for British children, including children whose rate of growth differs from their peers. However, since North American children are taller and mature at a slightly faster rate than British children (Tanner and Davies, 1985), the method may be less reliable for American children. It is not an easy method to use, since the RUS bone age estimation requires more time and effort than the Greulich-Pyle method, and prediction requires calculation with a regression equation. Like the RWT method, the TW2 method may result in predictions for older children which are less than their current heights.

4. Other Methods

Wilson et al. (1987) recently published a method for

predicting adult height for adolescents which incorporates a "Sexual Maturity Index" (SMI). The SMI is the patient's mean Tanner stage, and is used to adjust the patient's height percentile for rate of pubertal maturation. It is assumed that subjects maintain their adjusted height percentile through adolescence to adulthood. To estimate adult height, this percentile is extrapolated on a growth curve derived from data from 6768 healthy U.S. adolescents examined during 1966-1967 as part of the National Health Examination Survey. The final adult heights of these subjects were not available, so the SMI method was compared to the BP and RWT methods to assess reliability. For boys, the SMI method predictions exceeded those of the standard methods by an average of 1.9±5.4 cm (BP method) and 1.8±4.9 cm (RWT method). The SMI predictions were less than those of the standard methods for girls, by an average of 1.9±2.8 cm (BP method) and 5.1±3.7 cm (RWT method).[1] This method applies to both sexes from 12-17.5 years.

The ease and relative lack of expense necessary to use this method are advantageous (no x-rays are necessary, and all data can be obtained during one examination). The method applies to a clinically relevant age group. Disadvantages include the fact that final adult heights were not available to check the accuracy of the method, and no data are yet

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[1] Standard deviations of mean prediction errors indicated by ±.

available on the accuracy of this method for children with growth disorders.

An earlier method which incorporated information about sexual development was that of Onat (1983). This method allows estimation of adult stature in girls, using height, midparental stature, Greulich-Pyle bone age, whether or not Tanner stage 2 has been reached, and whether or not menarche has occurred. (Weight was used in the multiple regression analysis, but was found to be noncontributory, and was dropped.) The standardizing sample consisted of 100 Turkish girls, mostly of high socioeconomic status; however, in some age groups, fewer girls were enrolled (17 girls at age 9.0). The method may be applied to girls ages 9.0-14.0, with little growth expected after age 14. Accuracy of the method compares favorably with RWT for the standardizing group; however, no data are available from a validation group.

This prediction method appears to provide adequate accuracy; however, its use is limited to girls, and its applicability to Americans has not been established. Accuracy for early and late maturing children, and children with growth disorders is purely speculative. Since the RWT method can be used for a larger age range and for both sexes, clinicians are unlikely to switch to the Onat method with its more limited applications.

Pediatricians generally use growth curves as a screening tool to indicate disease, not for adult height prediction.

In one study, however, growth curves were used to predict adult height (Lenko, 1979). Termed the "relative height method", the child's height was simply plotted on a growth curve and extrapolated to the adult height corresponding to the same percentile. Although children are believed to follow their own "growth channels", this method did not lead to good predictions of adult height; substantial overpredictions occurred at all ages for normal children as well as boys with delayed puberty (Lenko, 1979). One possible reason for the inaccuracy of the relative height method was that the growth curve used in this study was derived from cross-sectional data (based on measurements of different children at each age) rather than longitudinal data (based on repeated measurements of the same cohort of children over time). Actual growth patterns are slightly different than those seen in cross-sectionally derived curves. This becomes especially important in adolescence because children progress through puberty at different rates.

Wilson et al. also used this method (called the "chart method") for adult height prediction and compared it to the SMI, BP, and RWT methods (Wilson et. al, 1987). They found the method to be quite accurate for adolescents maturing at the average rate; however, large errors were found when the method was used for children maturing either faster or shower than the middle group.

A series of growth curves for North American children

was developed by Tanner and Davies (1985) which was based on longitudinal data and therefore better represents the actual shape of individual growth curves. The curves derived from cross-sectional data by the National Center for Health Statistics (Hamill et al., 1979) were shown to overestimate height for average boys by 2 cm at 13 years, and underestimate by 2 cm at 15 years. Tanner and Davies also constructed separate growth curves for early and late maturers (for whom the cross-sectional data are even less accurate). These curves are designed for use in following children´s growth, not for predicting adult height. No studies are available which test the accuracy of the "chart method" with these growth curves.

Walker developed a method of height prediction in order to provide standards for somatotyping children (Walker, 1974). This method was developed from longitudinal data from healthy New Haven children (143 boys and 80 girls). Equations were derived using three combinations of variables: height and age alone, height, age, and growth rate over the preceding year, and the latter plus determination of whether or not the subject had passed his age of peak growth velocity. Predictions can be made for boys and girls from 2 to 20 years. The average error in the validation sample was 2-3 cm in boys from 9-14 years and girls from 8-12 years (Walker, 1974). No data were found regarding the use of this method in other populations.

The first method of height prediction specifically for girls with Turner's syndrome was based on data from four series of patients studied in Europe (Lyon et al., 1985). A total of 366 patients (both 45X and mosaic) from Germany, Finland, and France were included. A growth curve was obtained from the pooled data, and a regression equation derived for prediction. The only parameters necessary to use this method are age and height. The method was verified with data from 29 British patients who had been followed from childhood to age 19 to 24 years, and found to provide an adult height estimate with 95% confidence limits of the order of $\pm$2.0 cm. For 12 girls who had bone ages done at the time of initial evaluation, the method was found to be more accurate than the TW2 method: TW2 gave a mean error of +3.3 cm (overprediction), compared to the mean error of the Lyon method of -0.6 cm (underprediction). The method can be applied to Turner's syndrome patients of all ages. No significant differences in mean height were found in this study between 45X and mosaic karyotypes. The applicability of the method to U.S. patients with Turner's syndrome has not been established; however, it is almost certainly more accurate than prediction methods which were developed using normal children.

C. Comparison of methods of height prediction

There have been several studies where the various

methods of height prediction have been applied to non-standardizing groups. These studies may be used to estimate the bias associated with prediction methods, thereby allowing corrections to be made when the method is applied to a non-standardizing group.

In one study, a series of 60 healthy Finnish children (30 girls and 30 boys) was followed yearly from age 7 to 17 years (Lenko, 1979). A second series of 7 healthy boys with familial delayed growth and puberty was followed in an Endocrine Clinic. The adult heights of these patients were compared to their predicted heights obtained using the following methods: BP, RWT, TW1, Walker, "Relative Height" (RH) method (described above), and "Index of Potential Height" (IPH) method (identical to the RH method except bone age was used instead of chronological age; referred to in this thesis as the "Genel/Lenko Method"). The Finnish growth standards used for the RH and IPH methods were cross-sectional.

For the normal children, predictions with the BP, TW, and RWT methods were as accurate as for the standardizing series of the respective methods; the three methods were comparable in accuracy and precision. When bone ages were adjusted for differences between Finns and Americans, the IPH or Genel/Lenko method gave predictions comparable to the BP, TW, and RWT methods. For the boys with delayed growth and puberty, the corrected IPH, BP, and RWT methods gave the most

accurate results; all three methods were comparable and were more accurate than the TW method (Lenko, 1979). In a more recent study, 15 healthy Finnish boys with constitutional delay had adult height predictions made using the BP, RWT, and IPH methods (Lenko, 1982). The three methods were found to be comparable.

Harris and colleagues (1980) compared the BP, RWT, and TW (1975) methods using longitudinal data from healthy American children (22 boys and 24 girls). The mean prediction errors (predicted height minus adult height) and variances of the error for the three methods were generally equivalent; however, the mean error for the BP method was more symmetric about zero than for the other methods, and was associated with a larger error. The RWT and TW methods tended to underpredict (as did the BP method for girls 11-12 yrs). This underprediction was felt to be partially due to the use of adult heights obtained in the subjects' twenties, rather than stature at 18 years or stature obtained when the subject's yearly growth was <1cm. Underprediction of the TW method was attributed to differences between American and British children in rate of maturation which were reflected in the skeletal age estimates.

In a study of 56 normal Swiss children and 34 children with abnormal growth patterns, Zachmann and colleagues (1978) compared the BP, RWT, and TW1 methods of height prediction. The RWT and TW1 methods were found to be more accurate than

BP in normal children and in patients with familial tall stature. The BP method was felt to be preferable in conditions where decreased growth potential is untreatable, such as precocious puberty, Turner's syndrome, and primordial small stature. No statistics are given regarding the significance of the differences in accuracy between the various methods. The normal children were split into early-maturing, average, and late-maturing groups, but the data for each group are not presented.

So far, there are no published data on the reliability of the TW2 method, other than that of the authors. In all of the studies discussed above, earlier versions of the Tanner-Whitehouse method were used.

III. HYPOTHESIS

The Genel/Lenko Height Prediction Method

The prediction method proposed for this study (the Genel/Lenko, or GL method) has been used informally for many years in the Yale Pediatric Endocrinology Clinic as an adjunct to established prediction methods, primarily for counseling purposes. The method was first published by Lenko (1979), who called it the "Index of Potential Height" (IPH) method. This method is described on pp. 21-22. In the Lenko study, Greulich-Pyle bone ages of Finnish children were adjusted for differences between Finnish and American rates of skeletal development, and a Finnish growth curve was used. For the current study with American subjects, Greulich-Pyle bone ages and growth curves provided by the National Center for Health Statistics were used (Hamill et al., 1979).

The GL method is rapid, inexpensive, and easy (requiring no calculations or tables other than the growth chart), and can be used when other methods do not apply (e.g., wrong age group for BP tables, insufficient information for RWT). Experience with this method in the Yale Pediatric Endocrinology Clinic has produced the clinical impression that it is comparable to the established methods in accuracy, although it is probably associated with a larger error.

Lenko found the IPH (or GL) method to be comparable in accuracy and precision to the BP and RWT methods, and considerably more accurate than the TW method. For the same

population, predictions based on chronological age, height, and a growth curve (the "relative height" method) were inaccurate, indicating that the substitution of bone age for chronological age greatly improved the accuracy of prediction. This was true for normal children as well as for a group of boys with delayed puberty or delayed growth (Lenko, 1979). In a second study, the IPH method was again found to be comparable to BP and RWT for a group of boys with constitutional delay (Lenko et al., 1982).

Wilson et al. tested the "chart method" which is identical to the "relative height" method of Lenko, except for the use of growth curves derived from data from American children. They found that this method worked well for children maturing at the average rate, but the method produced large errors when used for fast and slow-maturing adolescents (Wilson et al., 1987). Wilson and colleagues corrected for different rates of maturation by incorporating the SMI rating in their method. The GL method is similar in concept: substitution of bone age for chronological age is essentially a correction for the variation in maturation rate which is seen in normal adolescents, as well as children with growth disorders. Since the majority of the children seen for growth evaluation are normal except for growing at a slower tempo (e.g., children with constitutional delay, delayed puberty), adjustment of the growth chart for bone age is expected to correct for this slower rate of maturation and

provide a reliable prediction of adult height.

While both of the Lenko reports consider the IPH method's applicability for boys with constitutional delay and delayed puberty, sample sizes were small and the method was not tested for girls or other groups of children with growth disorders. Wilson et al. tested their method on normal children only. In the current study of former patients in the Yale Pediatric Endocrinology Clinic, it is hypothesized that the GL method will provide accuracy comparable to BP and RWT methods for both sexes and a range of children with growth disorders. When applied to a wider range of children, the error associated with the GL method is hypothesized to be greater than the errors typically associated with established methods.

IV. MATERIALS AND METHODS

A. Study Design

Former patients who were seen in the Yale Pediatric Endocrinology Clinic for evaluation of short stature or growth failure were contacted and asked to provide a current measurement for this study. The charts of discharged patients were available beginning in 1971 (including patients who were initially seen before 1971, and were still being followed then). These charts were reviewed and potential subjects were selected who were born before 1967, were evaluated for short stature or growth abnormality (including tall stature), and had a bone age estimate. Due to time constraints, not all of the discharged patient charts were reviewed. They were reviewed alphabetically, with the A-M group completed.

A total of 338 letters were sent to former patients who fulfilled the above criteria. The initial letter (see Appendix A) was followed by a telephone call during which the former patient was invited to participate in the study. Subjects were encouraged to come to clinic to be measured; however, those who were unable to do so were measured at home and returned a postcard with the measurement. The majority (61%) of patients contacted by letter were lost to followup, either because of a change of address or telephone, or because the patient did not keep the clinic appointment or return the home measurement postcard. An adult height was

obtained from 35% of patients contacted. The rate of return of postcards was improved by contacting subjects a second time by telephone; however, due to time limitations, most patients were not reminded. The results of the original letters are shown in Table 1.

B. Measurements

Of the 22 patients for whom a "clinic measurement" was obtained, 19 were measured by the author in the Yale Children's Clinical Research Center, using the Harpenden stadiometer. The method described by Tanner et al. (1971) was used: gentle upward pressure was applied under the mastoid processes to obtain the child's maximum stature. This technique has been shown to minimize the decrease in height which occurs over the course of the day (Whitehouse et al., 1974). One subject was too tall to be measured with the Harpenden stadiometer; she was measured using a doctor's scale. For all of these measurements, the average of three heights was used. The other two "clinic measurements" had been obtained during clinic visits (these subjects were followed to ages 21 8/12 and 23 years). The measurements were verified by telephone in one case and home measurement in the other.

Home measurements were done according to written instructions which were patterned after the method used for the clinic measurements (see Appendix B).

C. Reported Height Data

For many subjects, a "reported height" was available as well as the measured height. This reported height was given by the subject or a family member before measurement was done. In order to determine the accuracy of such reported heights, the mean reporting error (reported height minus measured height) was calculated for subjects measured in clinic and those measured at home. The data are shown in Table 2. The reported heights given by subjects were found to be very accurate, with a mean reporting error of 0.1 in (standard deviation 0.7 in). Subjects who were measured in clinic were slightly more accurate than those measured at home in reporting their heights, but the difference was not significant. Because subjects were found to accurately report their heights, former patients for whom a measurement was not obtained (but a reported height was available) were included in the study. An additional 35 people who had reported an adult height, but did not provide a measurement, were included in the data base.

Reported heights provided by family members (usually parents) were found to be less accurate than those provided by subjects, with a mean reporting error of 0.4 in (SD 0.9 in). Reported heights obtained from family members were not used.

D. Diagnoses

Each patient's diagnosis was reviewed, and confirmed based on information in the chart. In cases where the working diagnosis changed after the initial evaluation, the revised diagnosis was used. Comprehensive reviews of diagnosis and treatment of growth abnormalities are available (Mahoney, 1987; Schaff-Blass et al., 1984). The most prevalent diagnoses in this series are listed in Table 3, and the principles underlying these diagnoses are reviewed briefly below. Although children diagnosed with constitutional delay, genetic short stature, and genetic tall stature are considered to have "growth disorders," these diagnoses actually represent normal variants. The classification of endocrinologically and genetically normal children into these categories is often based on judgement and clinical experience, rather than any clearly defined criteria.

1. Constitutional Delay

Children with constitutional delay are "late bloomers"; they mature slowly, completing their skeletal and pubertal development later than their peers. Birth weight is generally normal, with normal growth for several months followed by a decreased growth rate for several months. Growth velocity then increases and is normal for bone age during childhood, with the growth curve parallel to (and usually below) the fifth percentile. Bone age is roughly

equivalent to height age (the age at which the observed height is 50th percentile); both are significantly below chronological age. The adolescent growth spurt is delayed; however, final adult height and sexual development are normal. This diagnosis is more prevalent in boys than girls, and there is often a family history of delayed growth and development (Mahoney, 1987).

2. Genetic Short Stature

Genetic (or familial) short stature is diagnosed when there are parents or other healthy close relatives who are short, the child's projected adult height falls within 10 cm of the average parental height percentile, and the growth rate is normal. Birth weight tends to be low, but is consistent with the family history, and there are no findings suggestive of congenital dysmorphic syndromes. Turner's syndrome is generally excluded for girls. Bone age is consistent with chronological age, and height age may be several years younger than chronological age (Mahoney, 1987).

2. Constitutional Delay and Genetic Short Stature

Constitutional delay and genetic short stature may coexist in the same patient. In these instances, a family history of short stature and growth delay may be obtained. Bone age is less than chronological age, and height age is intermediate between the two.

3. Growth Hormone Deficiency

The diagnostic criteria for growth hormone deficiency

have undergone a revision in recent years. Classic GH deficiency is defined as a GH response of less than 7ng/ml following two standard GH stimulation tests (Wilson and Rosenfeld, 1987). Some children who are not classically deficient may show accelerated growth with GH therapy, however, it is not clear how to predict which nondeficient children will respond (Gertner, 1988).

4. Genetic Tall Stature

The vast majority of children who are evaluated for tall stature are female, presumably for social reasons. Genetic tall stature is accompanied by a family history of tall stature and a normal growth rate parallel to the median growth curve (and above the 95th percentile). Bone age is comparable to chronological age, and height age exceeds both of these values.

E. Predictions

For patients who had more than one prediction made, the first one was used. In a few cases, the first available prediction data were not applicable for all prediction methods (e.g., the bone age was too retarded for use in the BP method), so the earliest set of data which applied to the greatest number of prediction methods was used. Each prediction was recalculated, using data from the chart. The bone age values used for prediction were the values reported in patient charts; the films were not available for re-

reading.

Height predictions were carried out as follows:

1. Genel/Lenko Method

These predictions were obtained by following the procedure described on p. 24.

2. Bayley Pinneau Method

The tables provided by the authors (Bayley and Pinneau, 1952) were used.

3. Roche-Wainer-Thissen Method

The authors' instructions were followed as closely as possible (Roche et al., 1975). A few modifications were used as recommended. Parental heights were obtained by report instead of by measurement. Stature was converted to recumbent length by adding 1.25 cm. The value resulting from the regression equation (height at 18 years) was corrected to obtain "truly final adult height" since the study participants were selected for age greater than 20 years. The bone age used was that of Greulich and Pyle (1959), but was not the median bone-specific estimate recommended by the authors. Instead, it was obtained by comparison to radiographs representing modal skeletal development.

In three cases, population means were substituted for the heights of one or both parents, and in one case, the chronological age was substituted for bone age. All of these subjects were over 12 years old when the predictions were made; parental height and bone age are felt to contribute

little to accuracy of prediction at that age (Roche et al., 1975).

4. Other methods

The TW2 method was not used because the RUS bone age method is considerably more complicated than the Greulich-Pyle method. Most of the bone age films were not available for re-assessment using this technique, so it was not possible to test the TW2 method.

F. Statistics

For each subject, a "prediction error" (predicted height minus actual adult height) was calculated for each of the prediction methods used. Mean prediction errors and standard deviations were calculated for each method using standard statistical techniques. The mean prediction errors ($\pm$ one standard deviation) corresponding to various diagnostic groups were graphed for each method (see Figures 1-12). The absolute values of the individual prediction errors are plotted against age at prediction in Figures 13-18.

V. RESULTS

A. Study Participants

The diagnoses of participants in the study are shown in Table 3. The population from which these subjects were drawn has been characterized in a 1978 Yale M.D. thesis. This was a comprehensive review of the charts of patients who were evaluated for short stature during 1971-1976 (Finch, 1978). The patients seen during this time were diagnosed as shown in Table 4. Comparison of data in Tables 3 and 4 reveals that there are fewer boys with constitutional delay and combined constitutional delay and genetic (familial) short stature in this study than there were in those patients seen in clinic during 1971-1976. For girls, this study had about twice the expected number of constitutional delay subjects as expected from the Finch data, and far fewer combined constitutional delay and genetic short stature subjects. The number of subjects with genetic short stature appear to be comparable for both groups.

The reasons for these population differences are not clear. Because a significant fraction of the group being studied here was evaluated after 1976, recent changes in diagnosis could have contributed (e.g., changing criteria for diagnosing GH deficiency). There may also have been a diagnosis-related selection bias, with patients from some groups being less willing to participate in the study. The

most likely explanation, however, is that the differences are random, due to the relatively smaller sample in this study, and the large fraction of former patients lost to followup.

The mean age at prediction for boys was 13.7 (SD 2.1) years, for girls it was 12.9 (SD 2.1). The age distribution of study participants is compared to that of patients seen in clinic during 1971-1976 in Table 5.

The mean adult heights for study participants in the different diagnostic groups are shown in Table 6. Population means are included for comparison; most of the groups in this study attained a mean adult height within two standard deviations of normal for the general population.

B. Reliability of Prediction Methods

As shown in Figure 1, all three methods were found to overpredict for boys. When the boys who had a prediction made with all three methods were analyzed (Figure 2), the same trends are seen. The BP method is the most accurate, with a mean error of 0.3 inches, although the mean error for the RWT method (0.5 inches) is comparable, and the RWT method has a smaller standard deviation. The Genel/Lenko mean overprediction of 1.4 inches is considerably greater than those of the other methods. It also has a larger standard deviation.

Boys with constitutional delay represent the largest diagnostic group in this study. As shown in Figure 3, the

most accurate method of prediction with the smallest standard deviation is the RWT method. The BP method is reasonably accurate; however, the GL method has the largest error (overpredicts by 1.7 inches) and the largest residual (SD 3.0 inches). Even if the bias of the mean error were used to correct predictions, the large standard deviation makes this method less reliable than the other methods for clinical use. There was one subject in this group (J.C.) who was evaluated when he was only 5.9 years old, much younger than the rest of the boys with constitutional delay (for whom the mean age at prediction is 14.0 years, S.D. 2.2 years). Since the GL method overpredicted his adult height by 11.8 inches (compared to the mean prediction error of 1.7 inches), it was felt that this may have been due to inaccuracy of the bone age estimate at such a young age. Therefore, the boys with constitutional delay were analyzed without this subject; results are shown in Figure 4. The deletion of this subject decreases the mean prediction error for the GL and RWT methods (the subject was too young to have a BP prediction made but did have a RWT prediction); the effect is much greater for the GL method. (The error of this subject's RWT prediction was only 1.9 in.; the decrease from the GL error is probably due to the use of additional variables.) There is also a considerable decrease in the standard deviation for the GL method; a small increase is seen for the RWT method. In spite of these changes, the relative accuracy and

precision of the methods are the same: the RWT method is superior to both other methods, and the GL method is clearly inferior.

In contrast, for those boys diagnosed with both constitutional delay and genetic short stature, the Genel/Lenko method is roughly comparable to BP in accuracy and precision (see Figure 5). However, the RWT method was again found to be the most accurate as well as the most precise for this group, and would probably be the method of choice if convenience and expense were not a consideration.

For boys with genetic short stature only, the GL and BP methods provided comparable accuracy, with the BP method being slightly more precise (Figure 6). The RWT method has a greater mean error than GL, but precision of the two is comparable.

Results for boys with growth hormone deficiency are shown in Figure 7. Because this group was very small, the results are not very meaningful.

The data for all the girls in the study are shown in Figure 8; Figure 9 shows the results for girls who had a prediction made with each method. Differences between the two graphs are minimal. The GL and RWT methods were found to overpredict, while the BP method underpredicted by an average of 0.3 inches. All three methods have comparable standard deviations, which were smaller than those found for the boys for two methods (GL and BP); the RWT method was both more

accurate and more precise for the boys.

When analyzed by diagnostic group, there is no group of girls with more than 8 subjects, making it difficult to draw conclusions that are likely to be upheld in larger studies. Figures 10, 11, and 12 show the data for girls with constitutional delay, genetic short stature, and genetic tall stature respectively. The girls with genetic tall stature are the exceptions to every trend; this is the only group for which the GL and RWT methods do not overpredict and the BP method does not underpredict. Since this is the only group that was evaluated for tall stature, it is not surprising that the mean prediction error is in the opposite direction from that of the other groups.

It has been shown for all of the major prediction methods that accuracy improves with increasing age (Bayley and Pinneau, 1952, Roche et al., 1975, Tanner et al., 1983). As shown in Figures 13-18, the absolute value of the prediction error decreases with increasing age for all three methods being considered in this study. This decrease in error is much more dramatic for the boys than the girls. Since the data shown in Figures 13-18 are cross-sectional, they are more difficult to interpret than if they were longitudinal. (For example, someone whose prediction error was 5 inches when evaluated at age 14 may have had an even greater error if a prediction had been made at a younger age; the appearance of these graphs may be deceiving.)

C. Psychosocial Effects of Unusual Stature

While recruiting subjects for this study, an attempt was made to contact by telephone each of the 338 former patients to whom an introductory letter was sent. A variety of reactions was encountered when these former patients (or their parents) were reached. The vast majority of people were polite and helpful, and many were eager to discuss their experiences with growth evaluation and the adjustment to their height. During these conversations it became clear that for many patients the issue of stature had been one of acute importance during childhood and adolescence, sometimes continuing into adulthood. Because the comments from former patients and their families were completely spontaneous--no systematic effort was made to elicit them--the following observations are purely anecdotal. However, because psychosocial issues are so important in bringing many of these children to medical evaluation, it seems relevant to include this aspect of followup. The following discussion contains quotations which were generally taken from notes made during conversation; however, some were from memory, and were recreated to reflect the spirit of the remarks.

Although negative reactions were infrequent, when they occurred they tended to be quite strong. People who refused to participate in the study were more likely to express negative feelings about their adult height or their treatment

at Yale than those who agreed to participate. Almost entirely from males, negative responses were generally expressed as disappointment with not reaching the expected height. In one case, the subject had attained a height within the predicted range, but remembered the prediction as being greater than it actually was; he expressed feelings of having been misled.

A female participant, N., had been evaluated for short stature at age 17, after receiving hormonal therapy from another doctor to induce a growth spurt. She expressed strong concerns about the emotional aspects of this treatment. She said that her parents' concern about her appearance and desire to prevent her from having difficulties they experienced had led them to seek treatment which she felt was more detrimental than beneficial. The treatment included rhinoplasty to alter a nose which N. said "looked like Barbra Streisand's," and the hormonal treatment which was stopped when her voice became deeper. Fifteen years later, issues of body image appeared to still be salient. She said that she had become very close friends with a woman who was over 6' tall, partly because they shared many feelings about being different. N. expressed resentment of societal pressure to conform to others' expectations. While many of her concerns (unnecessary rhinoplasty, weight control) were not directly related to her short stature, she clearly considered them to be closely related.

J., a female who had been seen for short stature, said, "There is nothing wrong with me!" when first contacted. In spite of her assertion of normality, J. stated that her "children will be normal because their father will be over 6´ tall".

The parental desire to avoid bringing up painful memories of the short stature evaluation was apparent several times. One mother refused to tell her son about the study, saying, "Nothing was accomplished by his clinic visits, and he is still very sensitive about his height." She said that he has a Ph.D in Physics, is "brilliant", and she hopes "he finds a nice short girl!"

In spite of the perceived link between tall stature and success, the vast majority of former patients seemed to be leading active, productive lives involving school or careers, families, and community activities. (However there were two men in the sample who were unable to be measured because they were in jail.) The over-reporting of adult height, which one might expect in this population, was minimal (see Table 2). It was common for those who achieved their predicted height to be quite pleased, even if the prediction was relatively modest.

One mother of a boy with constitutional delay (who grew to 5´10") said, "We prayed every day that he would grow and now he´s taller than his dad! He owes it to Yale to come in and be measured."

Another boy with constitutional delay had several predictions made, and grew to 5´3", although most of his predictions were greater than this. He expressed very positive feelings about his care in clinic, and joked, "You should see my wife. She´s 6´2"!" (Coincidentally, his wife was encountered several weeks later, and was noted to be of medium height, perhaps 2-3" taller than her husband.)

G., a boy with constitutional delay who grew to 5´5", expressed satisfaction with his evaluation and treatment with oxandrolone. Although he was certainly informed at the time that oxandrolone would not increase his ultimate height, the growth spurt provided by the treatment was apparently beneficial. He was optimistic that height restriction would not prevent him from joining the police force.

The mother of S., a girl with genetic tall stature who had been called "Moose" in high school, described her daughter as a "stunning" woman who runs a lot, carries herself well, and models for a tall women´s clothing store. In spite of this excellent adjustment, when this mother reported a recent measurement of 6´1" she said she didn´t "want to know if S. is taller than this". Another girl with genetic tall stature exhibited a similar sort of denial when she said she did not believe a recent measurement of 5´8.5" and said that she had never wanted to be more than 5´8". When measured for this study, she was almost 5´9".

VI. DISCUSSION

The retrospective nature of this study imposed several methodological limitations. The following discussion outlines some of these.

A. Sources of Error, General

1. Skeletal Age Estimation

Many of the subjects in this study had bone age estimations done before coming to Yale for evaluation; variations in both technique and interpretation can be expected to result from this. (Outside bone ages were re-read by Yale radiologists whenever possible, but in a few cases the radiograph was not available, and the reported bone age was simply recorded in the chart.) As discussed above, bone age estimation is a subjective assessment requiring an experienced observer. A small difference in bone age may cause a large difference in height prediction, especially during the pubertal growth spurt. Many of the patients in this study were evaluated near the time of this growth spurt.

2. Error of Measurement

The error associated with measurements done in clinic using the Harpenden stadiometer is estimated to be less than 3 mm (Tanner and Davies, 1985). Each subject in this study was measured three times, and the measurements were always within this limit. Those subjects who were measured at home were asked to perform three measurements; not all subjects

did. However, among those who did report three measurements, they were consistently within a 0.25 inch range. The error associated with the non-measured heights (reported values) is expected to be greater than with the measured values; however, as discussed earlier, the reported heights were found to be quite accurate when both values were available (Table 2.)

3. Diurnal Variation

It is well known that height decreases as the day progresses. Ideally, all subjects would have been measured shortly after getting up, however, for practical reasons, this was not possible. About one third of measured patients (clinic and home measurements) were measured within 2 hours of getting up. The mean difference between morning and afternoon or evening heights has been reported to be 0.6 cm (0.2 in) in one study; other studies have found average differences of 0.2-1.54 cm (0.08-0.6 in) between morning and evening measurements (Buckler, 1978). Since most of the measurements done on children in the Pediatric Endocrinology Clinic were done more than 2 hours after arising, and these measurements were used to obtain the predictions, the degree of increased accuracy that could have been achieved by measuring the adult subjects early in the morning is probably not clinically significant.

4. Typographical Errors

Typographical errors and errors of transcription in the

medical records are inevitable. There was enough redundancy in the charts to allow several errors to be corrected, but it was not possible to double-check most of the data (such as heights and weights obtained during clinic visits).

5. Post-prediction events

Patients who experience a severe illness or accident after a prediction has been made might end up with an adult height that is quite different from the predicted height. For the patients in this study, a change in management of a disorder which resulted in growth evaluation might drastically alter the later growth. For example, a diabetic patient who was considered to be in good control at the time of her growth evaluation in early puberty later became less well controlled, possibly causing a decrease in adult height. Growth hormone deficient patients who become non-compliant or lose access to growth hormone (the patients in this study were receiving growth hormone when it was very scarce and sometimes unavailable) might experience a significant loss of growth potential as well.

6. Age

The participants in this study were older than those presenting for growth evaluation in the Pediatric Endocrine clinic. The mean age at height prediction in this study was 13.5 years, and the distribution of subjects by age is shown in Table 5. For comparison, this table also shows the age distribution of patients seen in clinic during 1971-1976.

The older age group represented in this study is believed to be due to the fact that the charts of discharged patients date back only to 1971. Patients born after 1967 were eliminated, so those who were seen more recently at a younger age were not old enough to be selected for the study, skewing the age distribution toward older patients.

Because the accuracy of height prediction improves with advancing age for every method (Bayley and Pinneau, 1952, Roche et al., 1975, Tanner et al., 1983), this age distribution may produce a false increase in accuracy of height predictions. This should not favor any one method more than the others; however, it does limit the conclusions that can be made about applying these methods to children with growth disorders who are younger than those included in this sample.

7. Use of Prediction Methods

Not all subjects had predictions made with each of the 3 methods being studied. If a particular subject was especially unusual (e.g., erroneous bone age, diagnostic error or aberrant growth pattern), and the data were applicable to only one of the methods, this could increase the mean error for that particular method. Such differences could have a significant effect in the smaller groups.

8. Population differences

The major difference between this series and the populations of normal children used to devise the published

methods of height prediction is that these children were diagnosed with growth disorders. Information is not available to retrospectively determine such characteristics as socioeconomic status, ethnicity, or other factors which may differentiate this study sample from the populations studied by others. In one study of 223 New Haven children, they were found to be taller than the U.S. national averages; however, the amount of this difference was not stated (Walker, 1974).

B. Sources of Error Specific to RWT method

All three methods being compared in this study used the subject's height at evaluation and bone age. The RWT method incorporates additional variables and therefore has more sources for potential error, although these parameters are not equally important at all ages.

1. Skeletal Age

The RWT method uses a bone age which is the median bone-specific Greulich-Pyle bone age estimate. Children with greater than 50% mature hand-wrist bones were excluded. Since the Greulich-Pyle bone ages used for the patients in this study were not estimated with the bone-specific technique, it is not known how many subjects were too mature to be evaluated with this method, or how much accuracy may have been lost by not using the bone-specific technique.

2. Parental stature

The authors of the method recommend measuring both parents and correcting heights to a "30-year value" (assuming a shrinkage rate of 0.06 cm/yr. for each year after 30). Because it was impractical to measure parents as well as subjects (and this was not a routine part of the growth evaluation in clinic), values reported in the chart or obtained by telephone were used. It was felt that many people do not revise their reported height for shrinkage after age 30, so that the reported values probably represent the parents' maximum heights.

Parents who experienced a severe illness or accident during childhood may not have attained their full height potential, thus causing a falsely low height prediction.

In three cases, one or both parents' heights were not available. As recommended by the authors, population means were substituted for the missing data. One of these children was diagnosed with genetic short stature, so the population mean may not be representative in this case. This is unlikely to have a significant effect on the overall accuracy of the RWT method, and in fact, is quite representative of the way this method is probably used in clinical practice.

Because parental height contributes little to overall prediction accuracy after age 16 in boys and 13 in girls, and the mean ages at prediction in this study were 13.7 and 12.9 for boys and girls respectively, these modifications of the procedure for determining parental height are not believed to

have significantly decreased the accuracy of these predictions.

3. Recumbent Length Correction

The mean difference between recumbent length and stature varies with age, and is different in different studies (reported range, 0.3-1.5 cm). There is evidence that the correction factor varies with different methodology, and should be established for each investigation (Roche & Davila, 1974). For this study, the correction factor recommended by the authors was used, since it was impossible to check retrospective data.

4. Weight correction for clothing

The authors of the RWT method recommend using a child's nude weight in the regression equation. The weights given in patient charts were not specified and were used uncorrected.

5. Adult Stature

Although the RWT regression equations specify stature at 18 years, the correction factors which provide final adult stature were used for this study. Since all of the patients in this study should have completed their growth (all but one were over 20 years and subjects who were aware of any growth over the last year were excluded), this seemed appropriate. However, the correction factors to final adult height may be misleading for subjects with growth disorders (i.e., correction may be too small for girls with genetic tall stature and too large for subjects with genetic short

stature). Since the correction factors are quite small (0.8 cm for boys and 0.6 cm for girls), this is not believed to have contributed a significant amount of error.

C. Sources of Bias

1. Agreement to Participate

Only a small fraction (4%) of those contacted actually refused to participate in the study. Reasons for refusal commonly seemed to involve feelings of disappointment in failure to achieve a predicted or desired height. In a few cases, the potential subject was never contacted because parents preferred to avoid bad memories associated with the clinic visits; some parents refused to tell the former patient about the study. For six of these non-participants, a reported height was obtained (usually from a family member); the mean reported height of these 6 male non-participants was 66.8 in (SD 3.2 in). Although this group is very small, their mean height is not significantly different from that of male participants (66.3 in, with SD 3.0 in) providing no evidence of a selection bias on the basis of height.

The number of people who agreed to participate but didn't was quite large. Some of these may have had negative feelings about their stature (perhaps the shorter ones) and therefore did not participate, creating a more subtle height-related selection bias.

D. Relative reliability of Prediction Methods

In order to be clinically useful, a prediction method must meet some standard of accuracy and precision. However, most authors do not quantify what they consider "adequate" accuracy or precision for a prediction method. For those methods which have been shown to have a known degree of bias in a given population, their utility may depend on the direction of that bias. For example, if two methods have the same mean error, but one overpredicts, and one underpredicts, they may not be equally useful. For children who are destined to be short adults, an erroneous overprediction may make adjustment to short stature more difficult. For children who are evaluated for excessive height, an underprediction may have a similarly adverse effect. Since so little published data are available on the accuracy of prediction methods for children with growth disorders, establishing stringent standards of accuracy is probably not warranted at this time. However, the relative accuracy and precision of the methods being considered can be evaluated.

The reasons for the discrepancies between the results of this study and those of Lenko (1979, 1982) are not known. Based on the Lenko work, the GL, BP, and RWT methods should provide comparable results for the boys with constitutional delay. As shown in Figures 3 and 4, the GL and BP methods are considerably less accurate and less precise than RWT. In

the Lenko studies, bone age estimates were done for the entire population by two individuals, whereas the bone age estimates used in the current study were assessed by many different readers, not all within the same institution. This could contribute to the greater precision of the GL method reported in the Finnish studies. In addition, the Finnish bone age estimates were corrected for known differences between Finnish skeletal maturation and the Greulich and Pyle standards, improving the accuracy of their predictions.

The Greulich and Pyle standards have been reported to be markedly advanced compared to the average maturity of American children (Roche, 1986). This would be expected to result in a bone age estimate which is more retarded than a child's true bone age, producing a falsely high adult height prediction in the GL method. In fact, the GL method was found to overpredict adult height for most groups in this study. It seems likely that correction of bone age standards and reducing the number of bone age readers would improve the method's precision.

These problems with bone age estimation would be expected to selectively decrease the accuracy of the GL method compared to the BP method, which was developed based on the Greulich and Pyle standards, so any differences between these standards and the population would be cancelled out. The RWT method employs a greater number of variables, so inaccurate bone ages would affect RWT predictions least of

all (especially at older ages, when bone age contributes less to overall prediction accuracy).

Zachmann and colleagues (1978) reported that the RWT and TW methods were better than BP for children with genetic tall stature. Review of their data reveals that the differences between the three methods were small, and the sample size was also small (5 boys and 6 girls). In this study, all seven of the genetic tall stature patients were girls, and the RWT and BP methods were roughly comparable. Both studies demonstrate a tendency for the RWT method to underpredict; this study showed overprediction of BP in contrast to the results of Zachmann et al., where the error of the BP method was symmetric about zero.

Because of the need for rapid followup, predictions are often used instead of actual adult heights to assess the effectiveness of treatment (Colle et al., 1977; Martinez et al., 1987; Schoenle et al., 1987). In such studies, it should be clearly stated that results are preliminary, awaiting the final adult heights. A treatment may alter height predictions without affecting adult heights. Likewise, predictions may not change with treatment but adult height may be affected (Martin et al., 1986). Because of the availability of GH in ample quantities, there will be greater need and opportunity to answer questions regarding the use of GH in nondeficient children and in Turner's Syndrome, and its optimal dose, frequency, and route of administration. Adult

height prediction will undoubtedly play a major role in answering these questions. In view of the results of this study, it seems prudent to recommend caution in interpreting results which are based only on changes in height predictions. Further study and refinement of prediction methods may allow their use in such studies; however, the best way to assess the efficacy of treatment is to obtain adult heights of treated and untreated patients.

E. Psychosocial Impact of Unusual Stature

Given the previously discussed evidence that short stature may impair personality development and result in overprotective parenting (Rotnem et al., 1977, 1979), it is not surprising that some of the former patients expressed negative feelings about their growth and that some parents refused to inform their children about the study. However, evidence of good adjustment to abnormal stature was more commonly encountered. Since most of the subjects attained a technically normal adult height (although many experienced a transient lag behind their peers), a good adjustment would be expected for this population as a whole.

VII. CONCLUSIONS

As hypothesized, the GL prediction method is associated with a larger error than the other two methods, and is not found to be the most precise prediction method for any diagnostic group. However, in contrast to the hypothesis, the GL method appears to be less accurate than the other two methods. For two diagnostic groups its accuracy was comparable to that of other methods (girls with genetic tall stature and boys with genetic short stature). For the largest group in the series, boys with constitutional delay, the GL method was the least accurate and least precise (Figures 3 and 4). The range of 67% confidence of 6 inches is too large to be desirable for clinical use.

In general, the Genel/Lenko method was found to overpredict; the only underprediction which occurred was for girls with genetic tall stature (Figure 12). In clinical practice, if the GL method were used, the BP method would probably also be used (it entails no additional expense and little trouble). The two methods tend to demonstrate opposing biases: when one overpredicts, the other underpredicts (with some exceptions for boys). Using both of these methods together could perhaps be helpful to clinicians who are aware of the biases, and could therefore arrive at an intermediate prediction estimate. The accuracy and precision of the GL method may be improved with more accurate bone age estimation (i.e., done at one center and read by a limited

number of experienced radiologists).

The BP method's accuracy compares favorably to RWT for both sexes in general and specifically for girls with constitutional delay. It was rarely demonstrated to be the most precise method, although its precision was comparable to that of the other two methods for girls. The BP method underpredicts for girls (except for those with genetic tall stature) and overpredicts for boys (except for those with combined constitutional delay and genetic short stature, genetic short stature, and growth hormone deficiency).

The RWT method is generally the most precise of the three methods compared in this study. This may be due in part to the large number of variables included in the RWT predictions. For boys, the RWT method is very accurate, and is the most reliable method for the groups with constitutional delay and combined constitutional delay and genetic short stature. However, the RWT method is never the most accurate method for girls in any diagnostic group and is the least accurate method for girls overall.

Based on the results of this study, the recommended prediction method for boys with constitutional delay and combined constitutional delay and genetic short stature is the RWT method. For boys with genetic short stature, the GL and BP methods are comparable, and when used together may provide the best results. For girls, the BP method is the method of choice since it appears to be the most accurate;

however, its precision is comparable to the other two methods.

The psychosocial aspects of growth evaluation appear to have played an important role in the personality development of the patient in this study. Although most subjects seemed to be quite well-adjusted, many subjects continued to have strong feelings about their size and/or treatment, even after many years. Effective counseling, including accurate adult height prediction, is therefore a necessary element of the management of children with growth disorders.

VIII. TABLES

Table 1. Results of Initial Letters Sent to Former Patients

	Number	Percentage
Data obtained from:		
clinic measurement	22	
home measurement	62	
reported height	35	
Total	119	35%
No data obtained:		
Refused to participate	13	4%
Lost to followup	206	61%
TOTAL contacted	338	

Table 2. Accuracy of Reported Heights vs. Measured Heights*

Height Reported by	n	Mean Measured Height (in)	Mean Reported Height (in)	Mean Difference Rept-Meas.(in)
Subject				
Verified in Clinic	19	64.2 (4.2)	64.4 (4.1)	0.0 (0.7)
Verified at Home	35	65.9 (3.9)	66.0 (3.8)	0.2 (0.8)
Total	54	65.4 (4.0)	65.5 (4.0)	0.1 (0.7)
Family Member				
Verified in Clinic	1	67.1	68.0	0.9
Verified at Home	15	67.4 (3.6)	67.8 (3.4)	0.4 (0.9)
Total	16	67.4 (3.5)	67.8 (3.3)	0.4 (0.9)

* Standard deviation in parentheses.

Table 3. Diagnoses of Study Participants

Diagnosis	Number		Percentage	
	Boys	Girls	Boys	Girls
Constitutional Delay	36	7	43	20
Constitutional Delay & Genetic Short Stature	18	1	21	3
Genetic Short Stature	16	6	19	17
Growth Hormone Def.	4	1	5	3
Genetic Tall Stature	--	8	--	23
Turner's Syndrome	--	3	--	9
Miscellaneous	10	9	12	26
Total	84	35		

Table 4. Short stature patients, 1971-1976

Diagnosis	Number		Percent	
	Boys	Girls	Boys	Girls
Constitutional delay	159	12	61	11
Familial Short Stature	44	22	17	20
Familial Short Stature and Constitutional Delay	34	45	13	42
Constitutional/Primordial /Idiopathic Short Stature	22	16	8	15
Chromosomal	1	13	<1	12
Total	260	108		

Table 5. Age Distribution of Study Participants

Age Group	Number	Percent
2-8 yrs.	1	1
8-14 yrs.	67	56
14-18 yrs.	51	43
Age Distribution of Clinic Patients, 1971-1976*		
2-8 yrs.		31
8-14 yrs.		44
14-18 yrs.		25

* data from Finch, 1978

Table 6. Mean Adult Height by Diagnosis

Diagnosis	Mean Adult Height in inches* Boys	Girls
Constitutional Delay	68.1 (2.7) [36]	62.6 (1.7) [7]
Constitutional Delay and Genetic Short Stature	65.9 (1.8) [18]	60.6 -- [1]
Genetic Short Stature	64.5 (1.9) [16]	58.7 (1.0) [6]
Growth Hormone Deficiency	66.1 (1.6) [4]	62.0 -- [1]
Genetic Tall Stature	--	71.5 (1.8) [8]
Other	63.9 (4.0) [10]	59.0 (2.8) [12]
TOTAL	66.3 (3.0) [84]	62.6 (5.4) [35]
U.S. General Population*	69.6	64.4

* standard deviation in parentheses (); sample size in brackets[]

* mean adult height at 18 years; from Hamill et al., 1979

IX. FIGURES

LEGEND

Figures 1-12. The mean prediction errors (± one standard deviation) corresponding to each diagnostic group are plotted according to method. Overpredictions (predicted height greater than actual height) are positive; underpredictions are negative.

Figures 13-18. The absolute value of the individual prediction error for each participant is plotted against age at prediction, for each of the three prediction methods.

Figure 1

All Boys

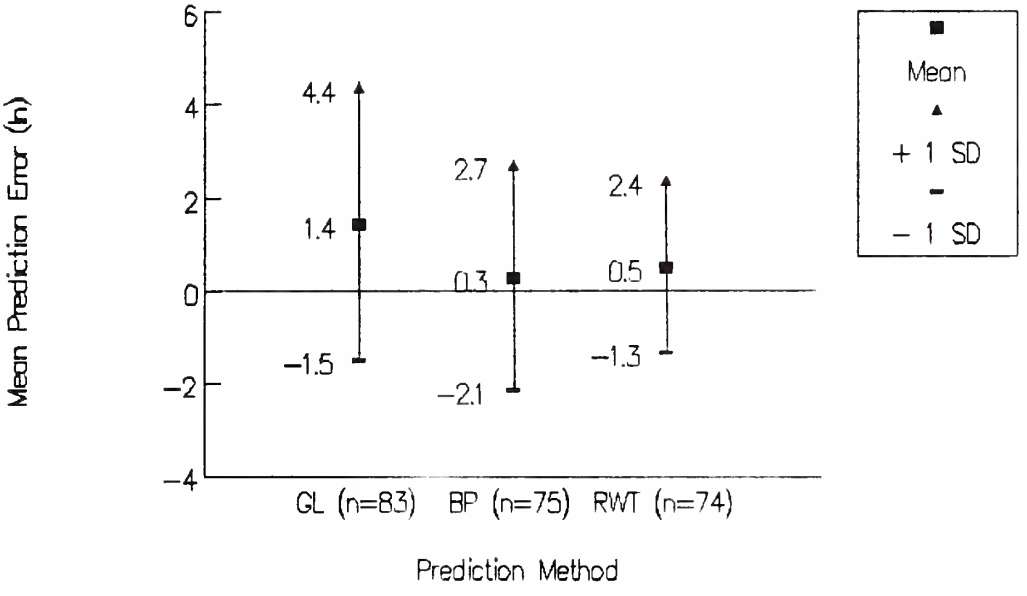


Figure 2

Boys with Three Predictions

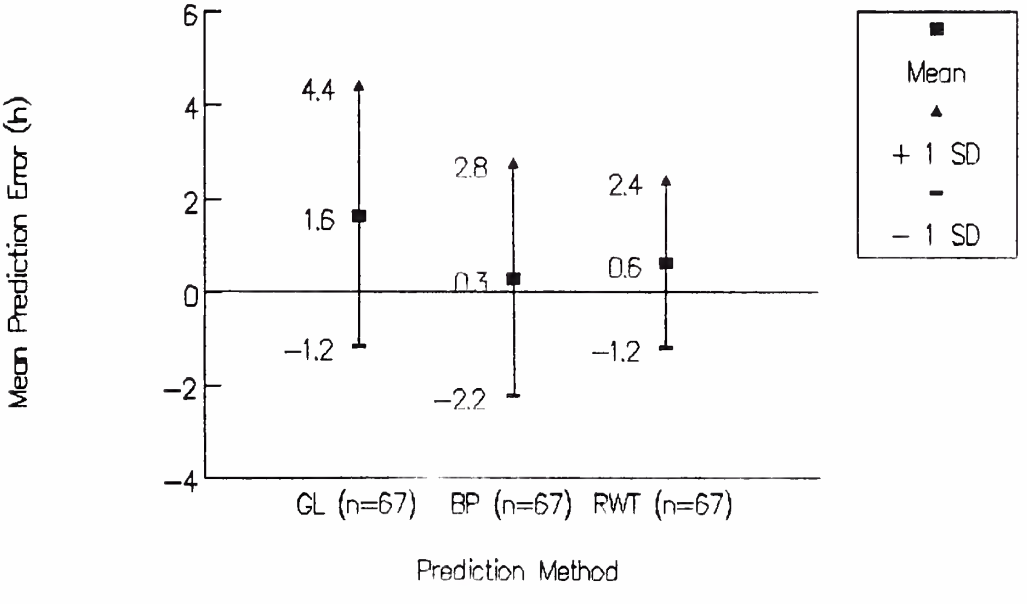


Figure 3

Constitutional Delay, Boys

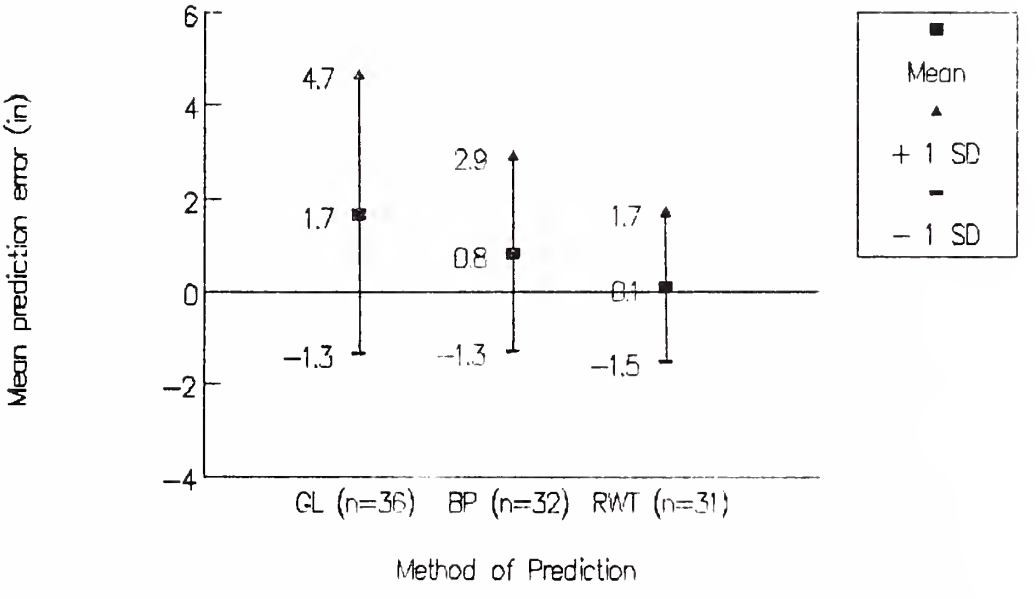


Figure 4

Constitutional Delay, Boys > 6 Yrs.

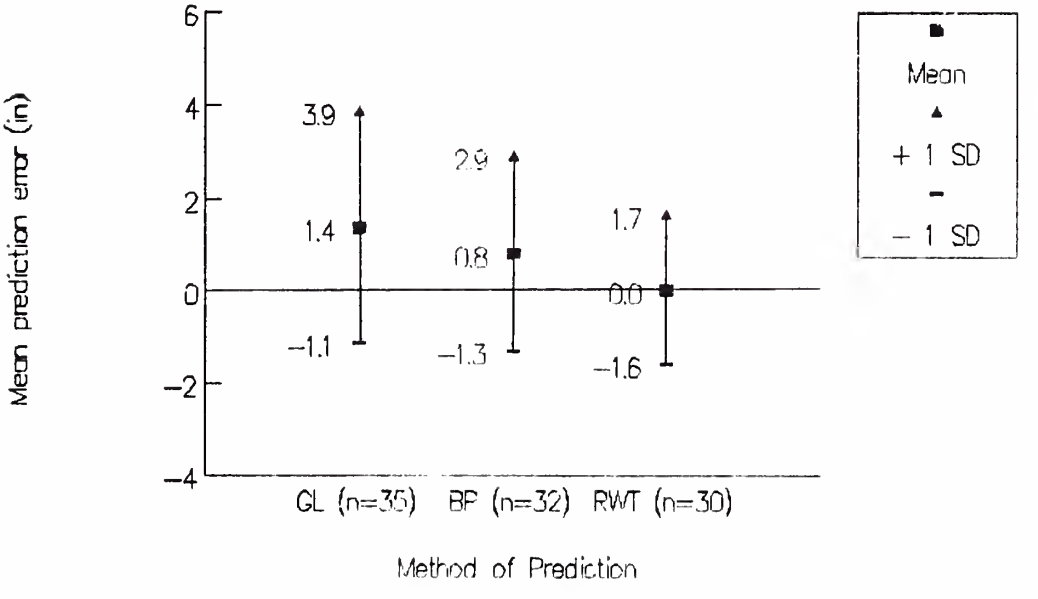


Figure 5

CD and GSS, Boys

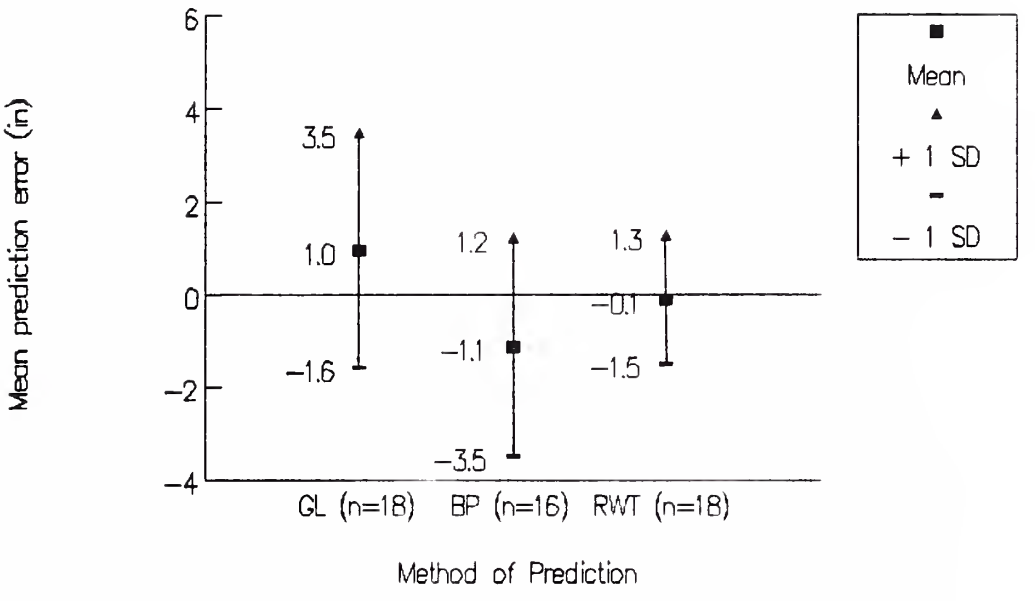


Figure 6

Genetic Short Stature, Boys

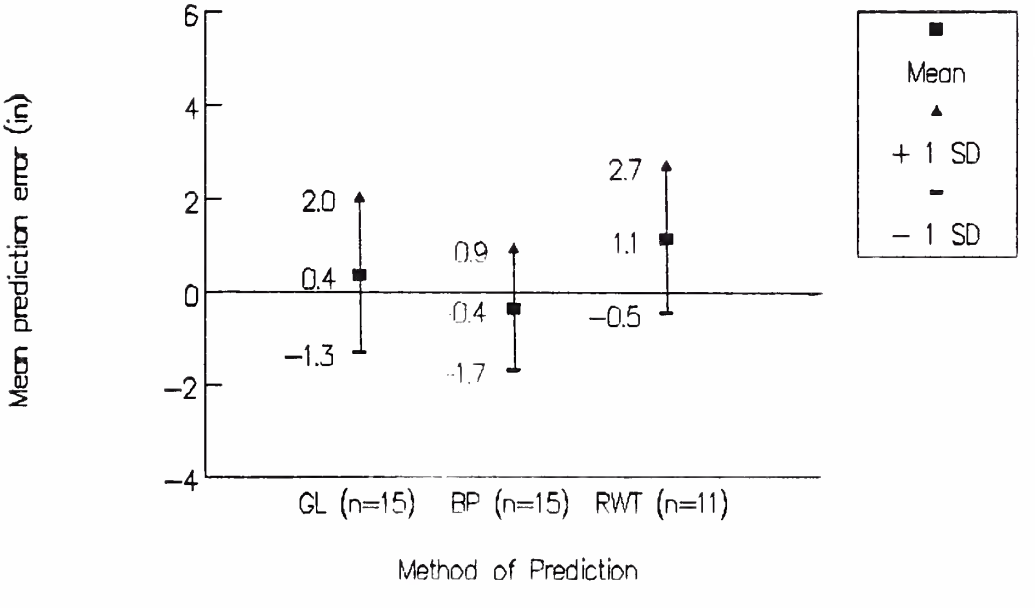


Figure 7

Growth Hormone Deficiency, Boys

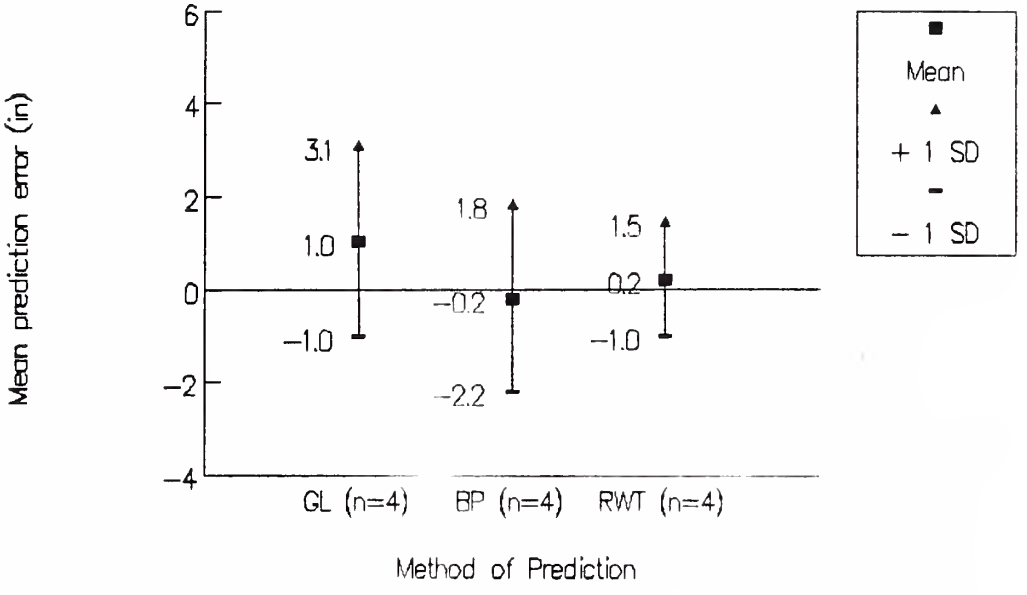


Figure 8

All Girls

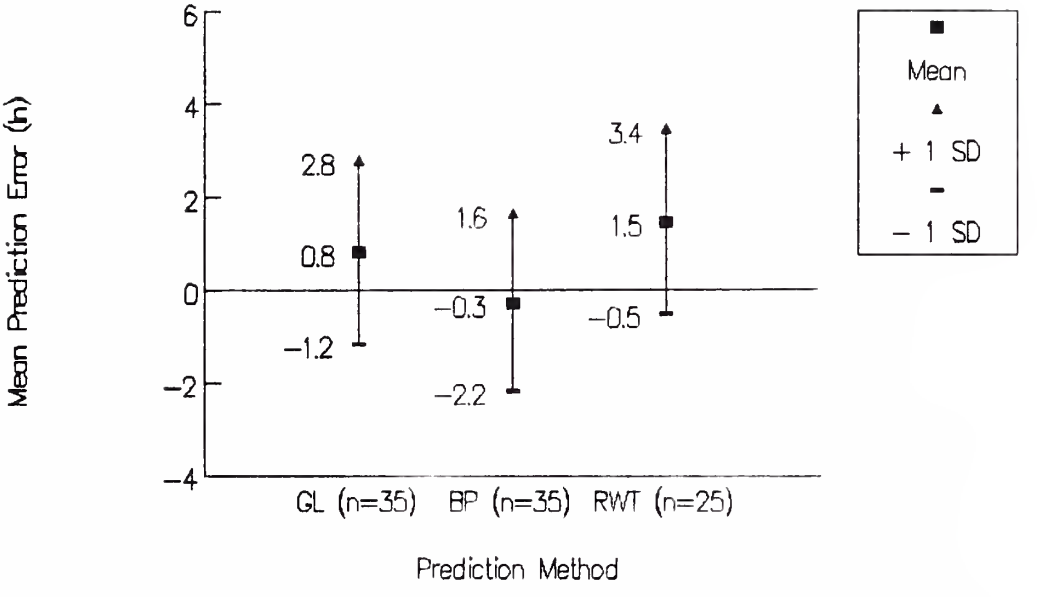


Figure 9

Girls with Three Predictions

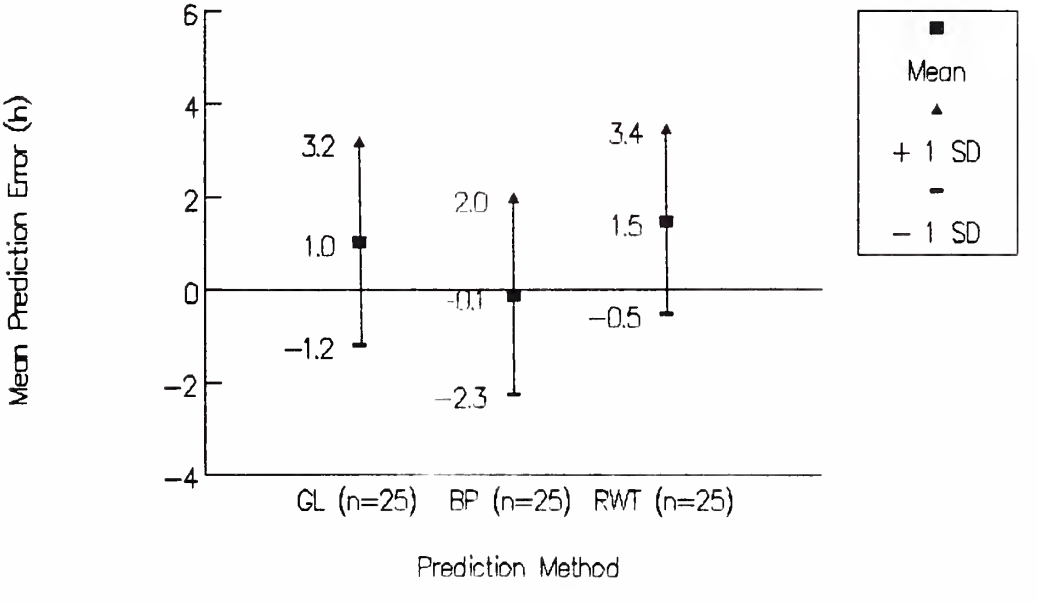


Figure 10

Constitutional Delay, Girls

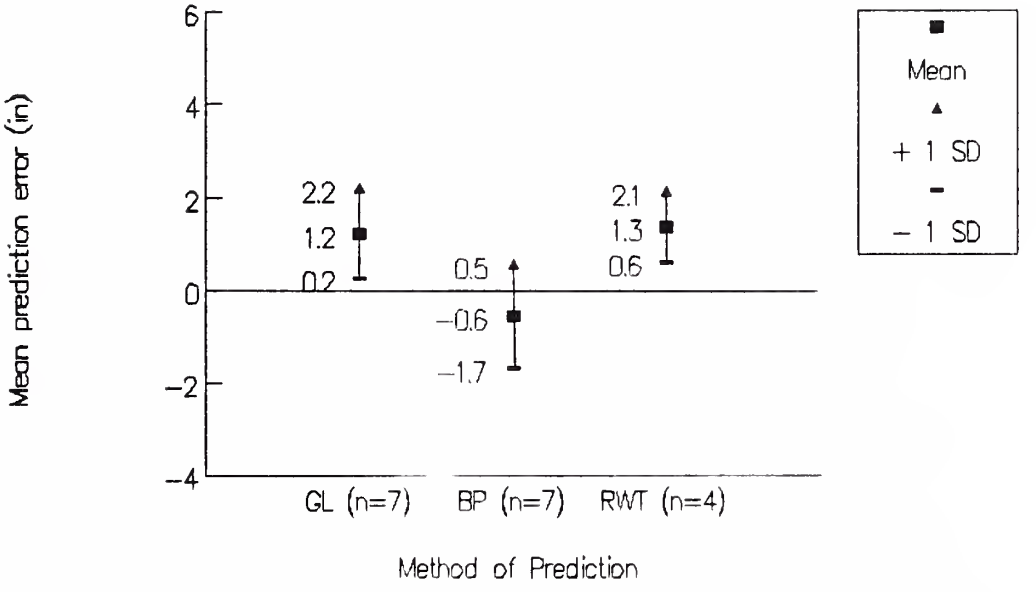


Figure 11

Genetic Short Stature, Girls

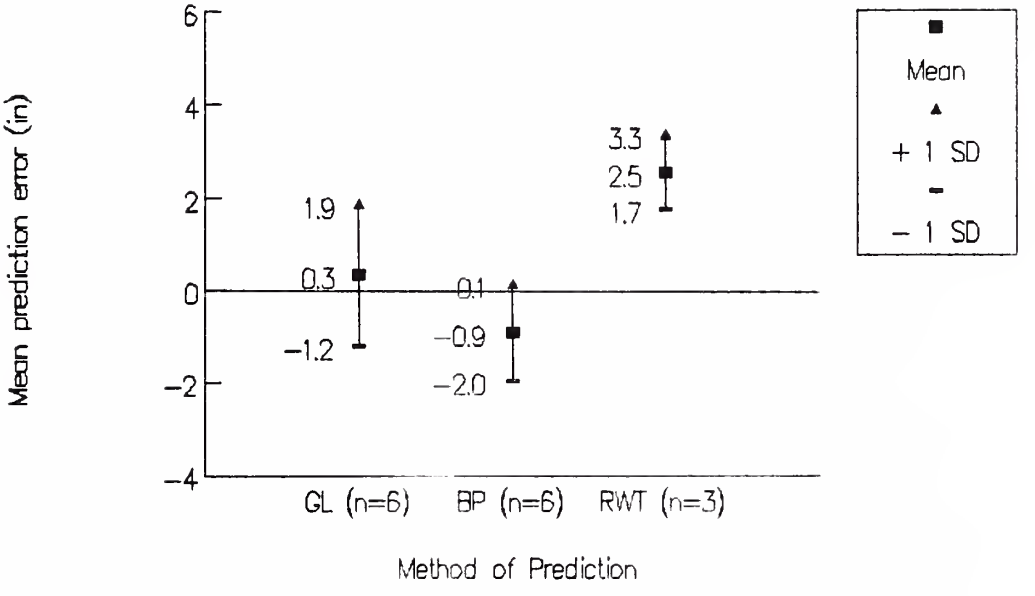


Figure 12

Genetic Tall Stature, Girls

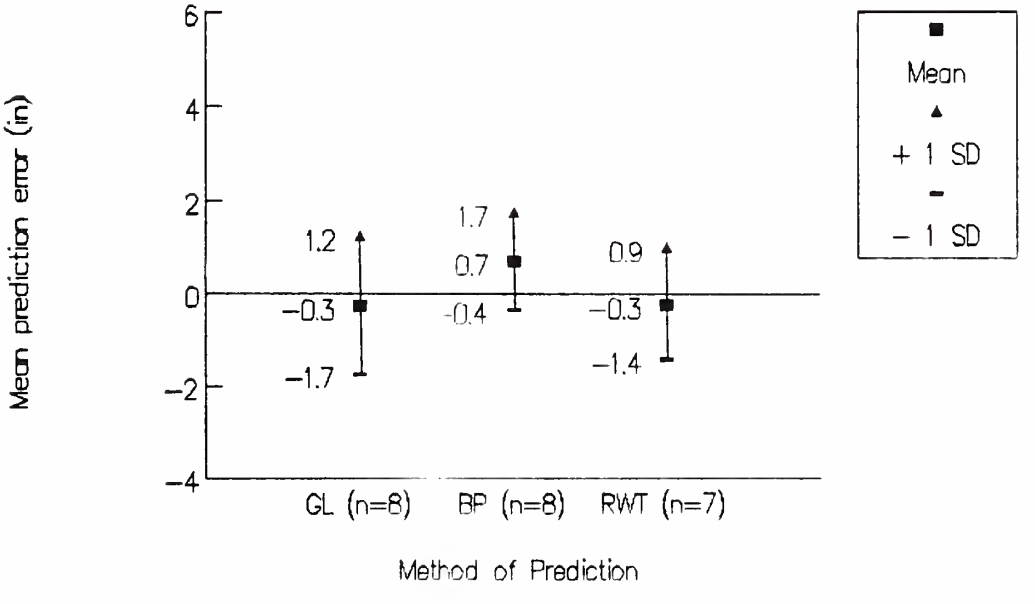


Figure 13

Genel/Lenko Method, Boys (n=82)

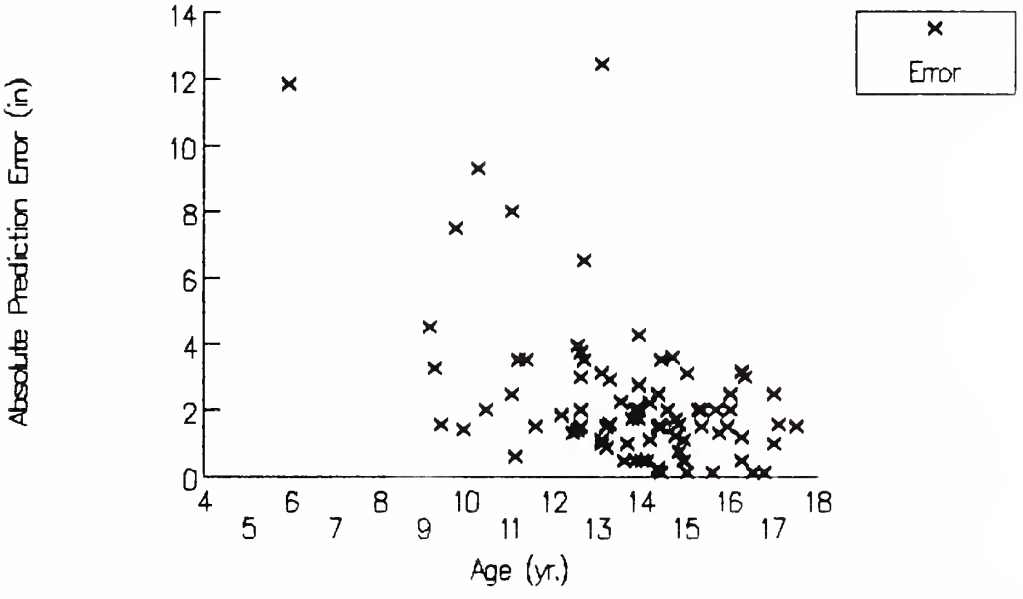


Figure 14

BP Method, Boys (n=75)

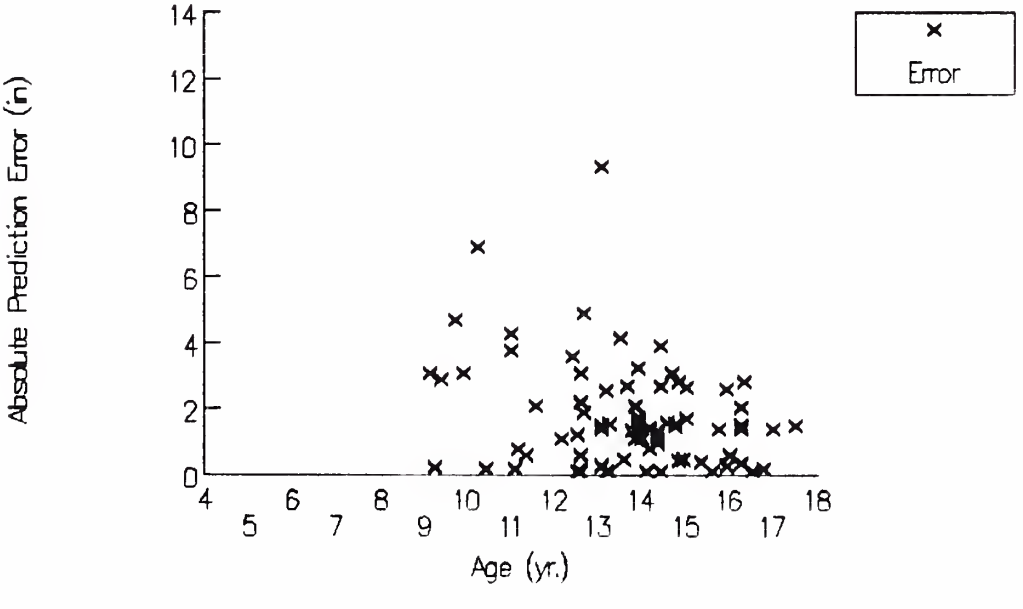


Figure 15

RWT Method, Boys (n=73)

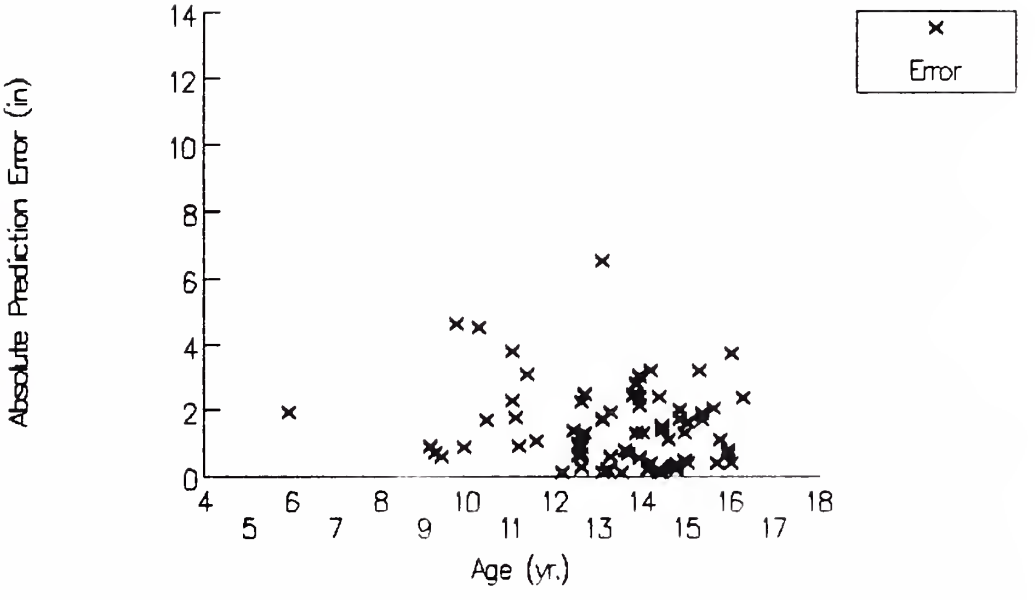


Figure 16

Genel/Lenko Method, Girls (n=35)

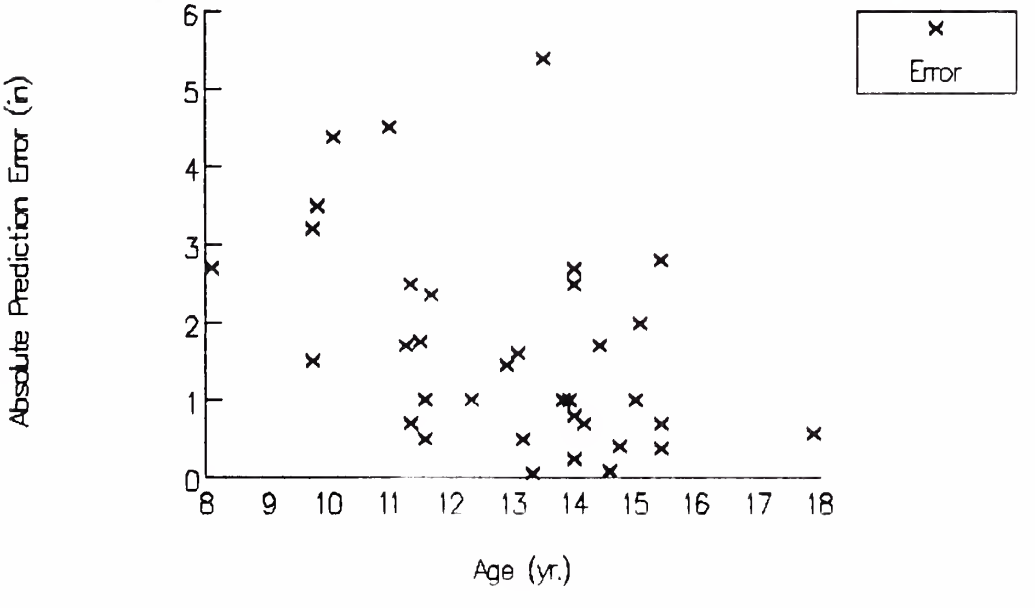


Figure 17

BP Method, Girls (n=35)

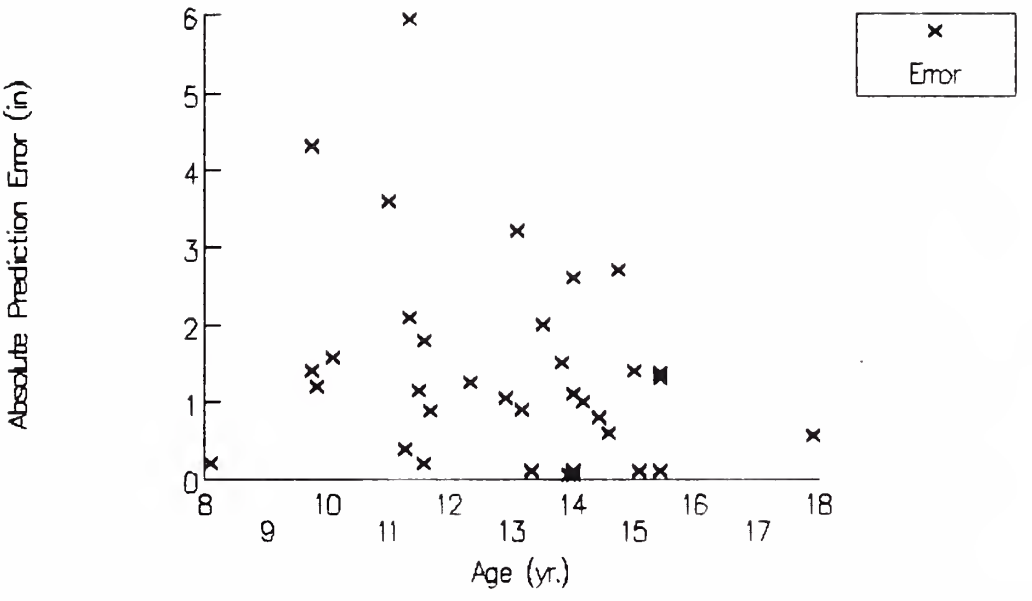
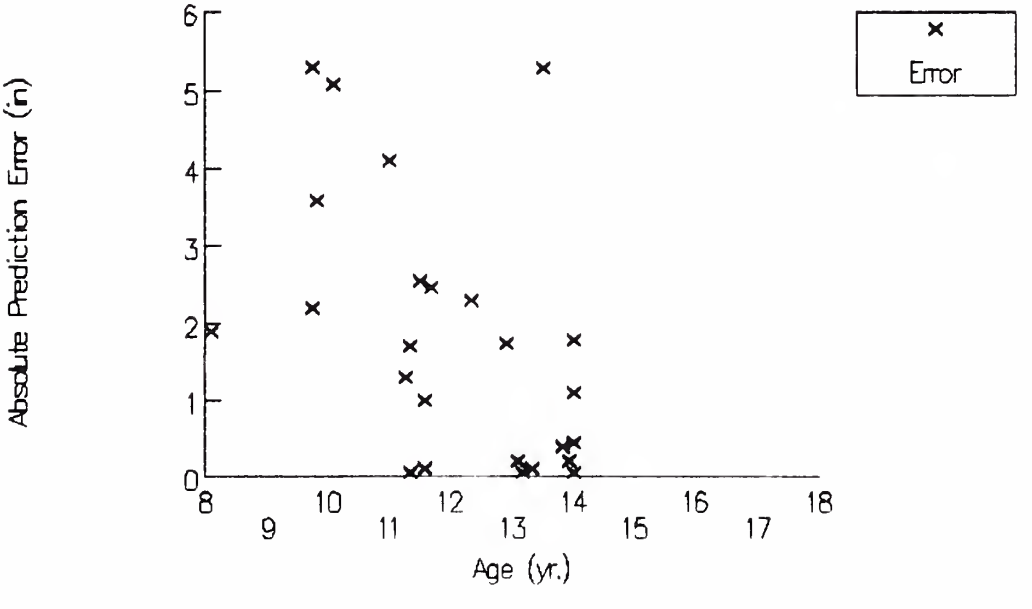


Figure 18

RWT Method, Girls (n=25)



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XI. APPENDICES

APPENDIX A Introductory letter sent to former patients

YALE UNIVERSITY
SCHOOL OF MEDICINE

SECTION OF PEDIATRIC ENDOCRINOLOGY
DEPARTMENT OF PEDIATRICS
P.O. BOX 3333
NEW HAVEN, CONNECTICUT 06510-8064
AREA CODE: 203 785-4648

82A

WILLIAM V. TAMBORLANE, JR., M.D. *Director*

MYRON GENEL, M.D., Assoc. Dean
MARTIN PRESS, M.B., M.R.C.P.
THOMAS CARPENTER, M.D.
FLORENCE COMITE, M.D.
PATRICIA DAVIS, R.N., M.S.N.
CYNTHIA TORONY-GRANFIELD, R.N.
BETH REILLY-ROMAN, R.N.

Because you were seen in our clinic for evaluation of your growth several years ago, we are writing to you now to request your help in a study of growth in children. We are trying to determine the best way to predict a child's adult height, in order to give the best advice to children we see now. Since we know what your adult height was predicted to be when you were seen in clinic, we would like to know your actual adult height for comparison.

The best way to obtain your current precise height is for you to come to clinic to be measured. This visit will be very brief, and will help us immensely. There will be no charge for this visit. If you are unable to come for measurement, you can still be of help by having someone measure you carefully at home, and sending us the result. All results of this study will be completely confidential.

We will call you within two weeks to answer any questions you may have and invite your participation in the study. You are free to decline without affecting your current or future relationships with doctors at Yale New Haven Hospital.

Thank you in advance for your cooperation.

Sincerely yours,

Irene Freeman
Yale Medical Student

Myron Genel, M.D.
Professor of Pediatrics

APPENDIX B Home measurement instructions

HOME MEASUREMENT INSTRUCTIONS

Please follow these instructions as carefully as possible; this will provide the most accurate measurement and ensure that all subjects in our study follow the same procedure. We ask you to do the measurement 3 times, as a check of your original measurement. Do not be concerned if the 3 values differ; this is to be expected, and we will use the average.

Because people may shrink as much as $\frac{1}{2}$" over the course of the day, the best time for measuring is early in the morning, within an hour of getting up. Please record the time of day the measurement was done, and how long you had been out of bed at that time.

1. Take your shoes and socks off and choose a wall with a bare floor. If you can find a spot with a vertical line on the wall (e.g. a wallpaper seam), this can serve as a guide to keep the tape measure straight during measurement.

2. Stand as straight and tall as you can, with your head and back against the wall. The heels of your feet should be together and touching the wall, and you should be looking straight ahead.

3. Have the measurer put his hands on your lower jaw, right in front of your ears, and with gentle upward pressure pull your head up. This stretches your backbone to achieve your full height.

4. Have the measurer place a flat surface (e.g. book, board) on top of your head and perpendicular to the wall. It is very important to hold the surface perpendicular to the wall (parallel to the floor) because any small change in angle may cause a significant change in the measurement. If the measurer is shorter than you, he should stand on a stool or chair in order to see well enough to be sure the surface is perpendicular to the wall.

5. With a soft pencil, make a small mark on the wall where the surface in contact with the head touches the wall.

6. Carefully measure the distance from the floor to the pencil mark, using a tape measure. Record measurement #1 to the nearest millimeter or nearest 1/8".

7. Erase the pencil mark and repeat the measurement twice; record these values. Fill out the enclosed postcard and mail.

Thank you very much for your help in our study of adult height prediction in children. You have been a big help!

APPENDIX C Data

Name	Sex	OPS #	dob	Dx	Height		Predictions			Differences			Age at pred'n
					(in)		GL (in)	BP (in)	RWT (in)	GL (in)	BP (in)	RWT (in)	(yr)
Clinic measurements (n=22)													
R.A.	M	097-12-82	092488	CD	70.4	C	72.0	70.5	69.8	-1.6	-0.1	0.6	13.3
R.A.	M	096-03-84	031363	CD	62.1	C	66.2	62.8	64.8	-3.1	0.3	-1.7	13.1
M.B.	M	093-07-18	110762	CD/GSS	67.1	C	68.5	65.9	68.1	-1.4	1.2	-1.0	12.5
S.B.	F	078-87-75	042760	CD	67.6	C	71.5	67.5	66.9	-3.9	0.1	0.7	13.5
R.B.	M	066-32-89	090460	4	58.6	C	71.0	67.9	65.1	-12.4	-9.3	-6.5	13.1
R.B.	M	097-86-50	020364	CD	66.1	C	69.0	67.6	68.0	-2.9	-1.5	-1.9	13.5
T.B.	F	101-55-55	053066	GTS	74.4	C	72.0	75.3	71.9	2.4	-0.9	2.5	11.7
S.C.	M	087-67-37	090860	GHD	67.1	C	68.0	69.7	67.3	-0.9	-2.6	-0.2	13.2
W.C.	F	091-66-26	012665	PGF	56.3	C	59.5	57.7	61.6	-3.2	-1.4	-5.3	9.8
A.C.	M	093-59-52	072060	5	65.9	C	69.0	68.5	67.5	-3.1	-2.6	-1.6	15.0
J.C.	M	070-23-23	091067	CD	62.2	C	74.0		64.1	-11.8		-1.9	5.9
T.C.	M	115-07-49	102966	CD	70.9	C	71.0	71.0	68.9	-0.1	-0.1	2.0	15.6
F.D.	M	057-19-74	041162	CD/GSS	66.6	C	68.0	63.5	65.7	-1.4	3.1	0.9	9.9
M.D.	M	067-10-01	071166	GSS	68.0	C	66.5	65.9	66.9	1.5	2.1	1.1	11.6
P.D.	M	087-33-58	030557	SS	63.8	C	65.0	64.2	66.2	-1.2	-0.4	-2.4	16.3
C.D.	M	089-16-18	121762	GHD	65.2	C	69.0	65.3	67.5	-3.8	-0.1	-2.3	12.6
M.E.	M	098-84-70	100967	CD/GSS	62.4	C	64.0	59.5	63.0	-1.6	2.9	-0.6	9.4
M.F.	F	094-36-52	121760	CD	64.8	C	64.4	62.1		0.4	2.7		14.8
J.G.	F	102-40-71	060265	CD/GSS	60.6	C	62.0	59.5	62.3	-1.4	1.1	-1.7	12.9
A.K.	F	085-86-56	010655	SS	57.4	C	58.0	58.0		-0.6	-0.6		17.9
G.K.	M	097-60-43	071967	CD/GSS	65.2	C	68.5	65.5	64.5	-3.3	-0.3	0.7	9.3
E.L.	F	105-40-56	093064	GSS	57.4	C	57.5	56.8		-0.1	0.6		14.6
		Avg, Clinic measured			64.6		67.0	65.0	66.3	-2.4	-0.3	-1.0	12.6
		S.D., Clinic measured			4.5		4.5	4.8	2.5	3.5	2.6	2.2	2.6
Home measurements (n=62)													
A.A.	M	088-27-95	071163	CD	65.2	H	74.5	72.1	69.7	-9.3	-6.9	-4.5	10.3
K.A.	F	113-76-16	071966	TS	57.7	H	60.5	59.0		-2.8	-1.3		15.4
C.B.	F	097-56-16	032765	1	65.0	H	66.0	65.2	64.9	-1.0	-0.2	0.1	11.6
J.B.	M	085-20-73	081959	CD/GSS	67.1	H	66.0	65.6	67.1	1.1	1.5	0.0	13.1
J.B.	M	107-60-40	120165	CD	67.5	H	68.0	67.4	67.3	-0.5	0.1	0.2	14.1
B.B.	F	084-79-04	110762	2	56.5	H	55.0	52.2	56.7	1.5	4.3	-0.2	9.8
S.B.	M	091-89-73	090863	CD/GSS	66.5	H	70.0	67.3	65.6	-3.5	-0.8	0.9	11.2
P.B.	M	106-36-06	060265	IBD/?CD	65.0	H	67.5	66.3	67.4	-2.5	-1.3	-2.4	14.3
S.B.	M	098-52-61	083860	CD	65.4	H	69.0	68.5	65.7	-3.6	-3.1	-0.3	14.7
J.E.	M	106-80-94	080967	CD/GSS	65.1	H	67.0	64.0	65.0	-1.9	1.1	0.1	12.8
R.E.	F	061-00-37	012761	TS	54.1	H	59.5	56.1	59.4	-5.4	-2.0	-5.3	13.5
C.E.	M	089-84-21	103061	CD	66.8	H	65.5	63.2	65.4	1.3	3.6	1.4	12.4
J.E.	M	095-73-39	050962	CD	71.3	H	69.5	69.8	70.7	1.8	1.5	0.5	13.9
M.E.	M	122-65-38	091767	CD	74.1	H	72.5			1.6			17.1
S.E.	M	105-27-03	071562	CD	66.9	H	70.0	68.9		-3.2	-2.1		16.3
S.E.	F	091-21-46	022163	GTS	73.0	H	73.5	74.8	72.0	-0.5	-1.8	1.0	11.6
J.E.	M	110-77-39	051266	CD	67.0	H	69.0	68.6	68.1	-2.0	-1.6	-1.1	14.6
E.G.	F	083-41-60	101260	GSS	59.3	H	60.0	57.2	61.0	-0.7	2.1	-1.7	11.3
A.G.	M	105-53-07	031667	GSS	66.3	H	65.0	64.0	64.4	-2.8	-1.8	-2.2	13.5
S.G.	F	070-19-98	010265	NF	59.8	H	62.5	60.0	61.7	-2.7	-0.2	-1.9	8.1
J.G.	M	067-74-23	091064	CD	67.3	H	71.5	70.5	70.3	-4.3	-3.3	-3.0	13.9
S.G.	F	100-11-66	080163	GTS	69.8	H	72.5	72.4	71.6	-2.7	-2.6	-1.8	14.0

K.C.	M	088-25-31	031461	CD	70.5	H	77.0	75.4	71.8	-6.5	-4.9	-1.3	12.7
J.D.	M	113-41-98	013165	GSS	60.5	H	60.5	60.7		0.0	-0.2		16.8
J.D.	M	101-50-58	042663	CD	71.8	H	73.0	73.3	71.4	-1.3	-1.5	0.3	14.8
T.D.	M	056-04-36	081359	GSS	64.3	H	66.5	65.1	67.5	-2.2	-0.8	-3.2	14.2
R.D.	M	099-24-41	091864	ISS	63.0	H	66.5	64.9	65.5	-3.5	-1.9	-2.5	12.7
J.E.	M	080-27-95	061063	CD	69.6	H	68.5	68.2	69.2	1.1	1.4	0.4	14.2
S.E.	F	093-88-67	090561	GTS	72.0	H	71.0	72.0	71.8	1.0	0.0	0.2	13.9
E.F.	F	104-68-60	111867	CD	63.8	H	65.5	63.4	65.1	-1.7	0.4	-1.3	11.3
K.F.	M	086-89-13	050457	CD	69.5	H	71.0	72.1	68.8	-1.5	-2.6	0.7	15.9
J.F.	M	085-78-46	012556	CD/GSS	67.6	H	66.0	64.8	65.6	1.6	2.8	2.0	14.8
K.F.	F	058-11-46	090762	NF	58.3	H	59.0	58.2		-0.7	0.1		15.4
L.F.	M	119-47-98	092366	GSS	65.0	H	64.0	63.6		1.0	1.4		17.0
B.F.	F	051-19-71	060759	GSS	60.4	H	60.0	59.0		0.4	1.4		15.4
D.F.	F	094-31-31	103161	CD	63.3	H	63.5	63.3	63.7	-0.3	-0.0	-0.5	14.0
J.G.	M	103-46-73	103163	CD	67.5	H	68.0	67.0	68.0	-0.5	0.5	-0.5	14.9
R.G.	M	104-45-79	022465	GSS	66.0	H	68.0	67.6	68.4	-2.0	-1.6	-2.4	15.9
J.G.	F	100-74-51	110866	EP	62.0	H	66.5	65.6	66.1	-4.5	-3.6	-4.1	11.0
J.G.	M	100-74-52	092364	CD	70.0	H	69.0	68.6	68.3	1.0	1.4	1.7	13.1
S.G.	M	114-75-24	080366	CD/GSS	66.0	H	68.0		66.4	-2.0		-0.4	15.7
D.G.	F	102-58-66	042564	GTS	69.7	H	67.0	67.9		1.7	0.8		14.4
D.G.	M	101-33-95	030363	CD	70.3	H	69.5	69.8	68.5	0.8	0.5	1.8	14.6
D.G.	M	067-97-07	091366	GSS	63.5	H	65.5	63.7	65.2	-2.0	-0.2	-1.7	10.4
D.G.	M	111-43-19	022367	GSS	65.8	H			65.0			0.8	
D.G.	M	110-38-26	021567	CD	67.3	H	69.0	68.6	69.7	-1.8	-1.3	-2.5	13.8
N.G.	M	084-20-81	031361	CD/GSS	64.5	H	65.0	64.0	65.3	-0.5	0.5	-0.8	13.6
F.H.	M	113-16-14	020569	CD	65.0	H	66.5	64.4	65.9	-1.5	0.6	-0.9	12.6
R.H.	M	093-47-20	091859	CD	67.2	H	68.5	68.6	66.1	-1.3	-1.4	1.1	15.8
P.H.	M	113-33-94	111366	CD/GSS	67.6	H	66.5		66.3	1.1		1.3	14.9
A.I.	M	075-48-03	032154	GSS	64.9	H	65.5	64.7	66.7	-0.6	0.2	-1.8	11.1
L.J.	F	106-79-95	091766	ASTHMA	61.1	H	59.5	57.9	61.3	1.6	3.2	-0.2	13.1
S.K.	F	094-31-35	071163	CD	62.8	H	63.5	61.8		-0.7	1.0		14.2
D.K.	M	059-15-05	030663	CD/GSS	67.5	H	66.0	64.8	66.0	1.5	2.7	1.5	14.4
K.K.	F	090-83-15	080463	TS	58.6	H	63.0	60.2	63.7	-4.4	-1.6	-5.1	10.1
V.K.	F	099-32-50	052363	GTS	72.8	H	72.0	72.9	72.8	0.8	-0.1	0.0	14.0
M.K.	M	085-43-38	092460	S	63.0	H	65.0		66.2	-2.0		-3.2	15.3
A.K.	M	118-41-38	122664	GSS	62.6	H	62.5	62.6		0.1	0.0		16.5
D.L.	F	070-84-39	101965	GTS	70.5	H	70.5	70.4	70.6	0.0	0.1	-0.1	13.3
P.L.	M	112-41-39	021966	GSS	64.5	H	66.5	64.1	66.5	-2.0	0.4	-1.7	15.3
T.L.	M	101-33-14	071064	CD/GSS	66.3	H	64.0	62.1	66.1	2.3	4.1	0.2	13.3
J.M.	M	061-11-15	111561	CD/GSS	65.8	H	66.0	64.8	65.9	-0.3	1.0	-0.2	14.3
		Avg., Home measured			65.5		66.7	65.6	66.8	-1.1	-0.2	-0.9	13.7
		S.D., Home measured			4.2		4.2	4.8	3.1	2.2	2.1	1.8	1.9
		Avg, total measured			65.3		66.8	65.4	66.6	-1.5	-0.2	-0.9	13.4
		S.D., total measured			4.3		4.3	4.8	3.0	2.7	2.2	1.9	2.2
Reported height (n=35)													
J.A.	F	091-57-54	041965	GSS	59.0	R	58.0	57.8	61.3	1.0	1.3	-2.3	12.3
J.A.	F	100-21-85	082362	GSS	58.0	R	57.0	56.6		1.0	1.4		15.0
T.A.	M	113-41-96	121267	GSS	64.0	R	66.0	65.1	66.9	-2.0	-1.1	-2.5	13.6
G.A.	M	069-14-80	042667	CD	67.5	R	69.0	68.6	67.7	-1.5	-1.1	-0.2	14.6
W.B.	F	103-52-50	061263	CD	59.0	R	61.0	59.1		-2.0	-0.1		15.1
K.B.	F	088-61-16	051167	HYPOPIT	61.0	R	58.5	54.9	61.0	2.5	6.1	0.0	11.3
R.B.	M	093-83-39	071964	CD/GSS	65.5	R	63.0	61.2	63.2	2.5	4.3	2.3	11.0
T.B.	M	079-41-92	010367	SHI	68.0	R	66.0	64.9	67.3	2.0	3.1	0.7	12.6

A.B.	M	114-19-24	092666	?CD	69.5	R	68.0		67.6	1.5		1.9	15.3
C.B.	F	064-35-18	061058	CD	63.0	R	65.5	64.1	64.1	-2.5	-1.1	-1.1	14.0
K.B.	F	102-05-92	012465	GTS	70.5	R	71.0	71.4	70.5	-0.5	-0.9	0.0	13.2
J.B.	M	095-56-91	010263	CD	68.5	R	70.0	68.6	68.7	-1.5	-0.1	-0.2	13.2
M.C.	M	100-51-14	122062	?GS	70.3	R	69.0	69.3	70.5	1.8	1.5	0.3	14.8
M.C.	M	085-26-80	010865	6	58.0	R	65.5	62.7	62.6	-7.5	-4.7	-4.6	9.8
G.D.	M	068-19-86	120660	7	61.0	R	64.5	61.6	64.1	-3.5	-0.6	-3.1	11.3
S.D.	F	065-14-39	092465	CD	61.8	R	63.5	60.6	64.3	-1.8	1.1	-2.5	11.5
M.D.	M	106-99-57	100364	CD/GSS	67.5	R	67.5	65.8	67.1	0.0	1.7	0.4	15.0
D.E.	M	102-76-16	070562	CD	71.0	R	68.5		67.3	2.5		3.7	16.0
S.D.	M	087-24-93	051561	GSS	67.5	R	64.5	65.3	67.2	3.0	2.2	0.3	12.6
D.F.	M	057-46-40	056662	CD	67.5	P	67.5	67.4	67.4	0.0	0.1	0.1	14.4
D.F.	M	056-54-32	111662	CD/GSS/	61.0	R	69.0	64.8	64.8	-8.0	-3.8	-3.8	11.0
R.F.	F	056-04-55	081062	GSS	58.0	R	61.5	59.2	61.6	-3.5	-1.2	-3.6	7.5
M.F.	F	089-64-06	110267	GHD	62.0	R	61.0	60.5	61.6	1.0	1.5	0.4	13.2
S.G.	M	043-01-84	112157	CD	68.5	R	68.0	67.4	67.2	0.5	1.1	1.3	14.0
C.G.	M	115-26-45	021866	CD	67.0	R	70.0	69.8		-3.0	-2.8		16.3
J.G.	M	087-78-86	071356	CD	72.0	R	69.5			2.5			17.0
W.H.	M	061-25-78	021864	GSS	66.0	R	65.5	63.9	64.7	0.5	2.1	1.3	15.8
R.H.	M	112-92-30	053165	CD	72.5	R	73.0	74.0		-0.5	-1.5		16.3
C.I.	M	084-35-34	041462	CD	67.5	R	72.0	70.6	66.6	-4.5	-3.1	0.9	9.2
M.J.	M	094-21-61	010362	CD	65.5	R	64.5	62.8	66.2	1.0	2.7	-0.7	13.7
F.K.	M	110-93-56	070463	GSS	62.5	R	61.0	61.0		1.5	1.5		17.5
K.K.	M	093-36-56	112359	CD	63.0	R	65.0	63.6	63.6	-2.0	-0.6	0.4	16.0
J.K.	M	042-70-01	093064	CD/GSS	67.0	R	70.5	70.9	68.4	-3.5	-3.9	-1.4	14.4
M.L.	M	117-04-66	090966	GSS	64.5	R	64.0	63.1		0.5	1.4		15.3
R.M.	M	053-26-08	041560	GHD	64.0	R	65.5	63.7	63.2	-1.5	0.3	0.8	15.9
		Avg., reported			65.1		65.8	64.4	65.6	-0.7	0.2	-0.4	13.8
		S.D., reported			4.1		3.9	4.5	2.7	2.7	2.3	1.9	2.1
		Avg., TOTAL (n=119)			65.2		66.5	65.1	66.3	-1.2	-0.1	-0.8	13.5
		S.D., TOTAL			4.2		4.2	4.8	3.9	2.7	2.3	1.9	2.2

C=clinic measurement
H=home measurement
R=reported by subject
F=reported by family member

CD=constitutional delay
GHD=growth hormone deficiency
GSS=genetic short stature
GTS=genetic tall stature
IBD=inflammatory bowel disease
ISS=idiopathic short stature
MISC
1=hypotpit, S/P cranio
2=multifocal eosinophilic granuloma with idiopathic short stature
3=Blackfan-Diamond Syndrome/CD/Steroid Rx
4=adrenal hypoplasia, hypogonadism (autoimmune)
5=thalassemia intermedia with delayed adolescence
6=?CD/primordial dwarfism
7=Noonan's syndrome
NF=neurofibromatosis
PGA=possible growth arrest
PGF=primordial growth failure
PP=precocious puberty

SS=short stature
TS=Turner's Syndrome

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